Suicidality in psychotic disorders; demographical, clinical, and neurocognitive correlates

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CONTENTS

ACKNOWLEGDEMENTS 4

SUMMARY 5

LIST OF PAPERS 7

ABBREVIATIONS 8

1. INTRODUCTION 9
1.1. Psychotic disorders 9
1.1.1. Definitions and classifications 9
1.1.2. Schizophrenia 10
1.1.3. First episode psychosis 12
1.2. Suicidality 14
1.2.1. Terminology 14
1.2.2. Prevalence of suicidal behaviour 15
1.2.3. The development from suicidal ideation to suicidal acts 17
1.2.4. Suicidality and psychiatric illness 18
1.3. Suicidality in psychotic disorders 19
1.3.1. Prevalence of suicidal behaviour in psychotic disorders 19
1.3.2. Non-fatal suicidal behaviour 20
1.3.3. Risk factors for suicidal behaviour in psychotic disorders 21
1.3.4. Neurocognitive function and suicidality in psychotic disorders 23
1.3.5. Early psychosis and risk for suicidality 26
1.3.6. Insight into psychosis 27
1.3.7. Beliefs about psychosis 28
1.3.8. Insight, beliefs about psychosis, and suicidality 29

2. AIMS OF THE THESIS 30

3. MATERIAL AND METHODS 31
3. 1. Setting 31
3.2. Design 31
3.3. Material 31
3.4. Methods 33
3.4.1. Clinical assessment 33
3.4.1.1. Diagnoses 33
3.4.1.2. Symptoms and functioning 33
3.4.1.3. Suicidality 34
3.4.1.4. Illness course 35
3.4.1.5. Demographical data, substance use, and medication 35
3.4.1.6. Beliefs about psychosis (Study III) 36
3.4.2. Neuropsychological assessment (study I) 36
3.5. Procedures 38
3.6. Ethical considerations 39
3.7. Statistical analyses 39

4. RESULTS/SUMMERY OF PAPERS 41
Paper I: Neurocognitive functioning and suicidality in schizophrenia spectrum disorders . 41
Paper II: Suicidality before and in the early phases of first episode psychosis 41
Paper III: Suicidality in first episode psychosis is associated with insight and negative beliefs about psychosis 42

5. DISCUSSION 44
5.1. Discussion of main findings 44
5.1.1. Neurocognitive functioning and suicidality in schizophrenia spectrum disorders..... 44
5.1.2. Suicidality before and in the early phases of first episode of psychosis 46
5.1.3. Insight, beliefs about psychosis, and suicidality in first episode psychosis 49
5. 2. Discussion of general methodological issues 50
5.2.1. Sample issues; representativity and generalisability 50
5.2.2. Design issues; cause and effect 55
5.2.3. Measurement issues; validity and reliability 56
5.2.3.1. General clinical assessment 56
5.2.3.2. Neuropsychological assessment 57
5.2.3.3. Assessment of suicidality 57
5.2.3.4. Measuring beliefs about psychosis 60
5.3. Strengths, limitations, and future research 60
5.4. Implications 63

6. CONCLUSION 64

7. REFERENCES 66
APPENDIX 1
PAPER I, II, and III

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SUMMARY

The overall aim of this thesis was to identify possible demographical, clinical, and neurocognitive risk factors for suicidal behaviour in patients with psychotic disorders.

Suicidal behaviour and neurocognitive impairment are serious and prevalent problems in patients with schizophrenia. Studies indicate that suicidality in patients with schizophrenia may be associated with relatively higher neurocognitive functioning, but the findings are few and inconsistent. Also, behavioural- and personality measures of impulsivity have been linked to increased suicidal behaviour in patients with schizophrenia, but this relationship has not been studied by neuropsychological measures. The first aim of the present thesis was to investigate whether suicide attempters had higher IQ, better executive functioning, or were more impulsive (had poorer inhibitory control) compared to non-attempters in a group of patients with schizophrenia spectrum disorders. The possible confounding effect of current suicidality was taken into account. In a group of 174 patients with schizophrenia spectrum disorders, we found that there were no difference between suicide attempters and non-attempters in IQ, executive function, impulsivity (inhibitory control), or any other neurocognitive domain. The presence of current suicidality did not confound the results. An interesting post hoc finding was that currently suicidal patients were more impulsive (had poorer inhibitory control) than currently non-suicidal patients, but this difference was mediated by positive psychotic symptoms.

The suicide risk in psychotic disorders is highest in the early phases of illness. Studies have typically focused on suicidality from treatment start rather than the actual onset of psychosis. Thus, the second aim of the thesis was to explore the prevalence and characteristics of patients with a first episode of psychosis and suicidality in two different time intervals: 1) prior to study entry and 2) explicitly in the period of untreated psychosis. In a sample of 170 patients with first episode of psychosis, we found that nearly 26% of the patients attempted suicide prior to study entry, and 14% made suicide attempts during the period of untreated psychosis. Of the patients who had been suicidal (i.e. experienced suicidal ideation or attempts), 70% were suicidal during the period of untreated psychosis. Suicide attempts prior to study entry were associated with female gender, more depressive episodes, younger age at psychosis onset, and history of alcohol disorder. Suicide attempts during untreated psychosis

were also associated with more depressive episodes and younger age at illness onset, in addition to drug use the last six months and longer duration of untreated psychosis (DUP).

Insight has been found to be associated with increased risk for suicidal behaviour, but not consistently. A possible explanation for this is that insight has different consequences for patients depending on their beliefs about psychosis. The third aim of this thesis was to investigate whether a relationship between insight, negative beliefs about psychosis, and suicidality was mediated by depressive symptoms, and if negative beliefs about psychosis moderated the relationship between insight and suicidality. In a sample of 194 patients with a first episode of psychosis, we found that nearly 46% of the patients were currently suicidal. Depressive symptoms, having a schizophrenia spectrum disorder, insight, and beliefs about negative outcomes for psychosis were independently associated with current suicidality; contradicting a mediating effect of depressive symptoms. Negative beliefs about psychosis did not moderate the effect of insight on current suicidality.

In conclusion, our results suggest that neurocognitive functioning is not essential for engaging in suicidal acts, at least not the neurocognitive domains measured in the present study. Furthermore, the prevalence of suicidality before and in the early phases of first episode psychosis is high, especially during untreated psychosis. As prolonged DUP is associated with suicide attempts during the period of untreated psychosis, reducing the DUP could have the effect of reducing the prevalence of suicide attempts in patients with first episode psychosis. Our findings also indicate that more depressive symptoms, higher insight, and negative beliefs about psychosis increase the risk for suicidality in patients with first episode of psychosis. This finding imply that monitoring insight should be part of assessing the suicide risk in patients with first episode psychosis, and that treating depression and counteracting negative beliefs about psychosis may possibly reduce the risk for suicidality.

LIST OF PAPERS

Study I
Barrett, E.A, Sundet, K., Simonsen, C., Agartz, I., Lorentzen, S., Mehlum, L., Mork, E., Andreassen O.A., Melle, I. Neurocognitive functioning and suicidality in schizophrenia spectrum disorders. *Comprehensive Psychiatry*, doi: 10.1016/j.comppsych.2010.06.001.

Study II
Barrett, E. A., Sundet, K., Faerden, A., Nesvag, R., Agartz, I., Fosse, R., Mork, E., Steen, N.E., Andreassen, O.A., Melle, I. (2010). Suicidality before and in the early phases of first episode psychosis. *Schizophrenia Research, 119,* 11-17.

Study III
Barrett, E. A., Sundet, K., Faerden, A., Agartz, I., Bratlien, U., Romm, K. L., Mork, E., Rossberg, J.I., Steen, N.E., Andreasen, O.A., Melle, I. (2010). Suicidality in first episode psychosis is associated with insight and negative beliefs about psychosis. *Schizophrenia Research,* doi:10.1016/j.schres.2010.07.018.

ABBREVIATIONS

ANOVA	Analysis of variance
CDSS	Calgary Depression Scale for Schizophrenia
C-W Interference Test	Color-Word Interference Test
CVLT-II	California Verbal Learning Test, second edition
D-KEFS	Delis Kaplan Executive Functioning Scale
DSH	Deliberate self-harm
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)
DUP	Duration of untreated psychosis
FEP	First episode of psychosis
GAF	Global Assessment of Functioning scale
ICD-10	ICD-10 Classification of Mental and Behavioural Disorders
IDS-C	Inventory of Depressive Symptoms – Clinician rated
ICC	Intraclass coefficient
IQ	Intelligence quotient
NART	National Adult Reading Test
PANSS	Positive and Negative Syndrome Scale
PAS	Premorbid Adjustment Scale
PIQ	Performance IQ
SCID-I	Structured Clinical Interview for DSM-IV Axis I Disorders
SCI-PANSS	Structured Clinical Interview for the Positive and Negative Syndrome Scale
VIQ	Verbal IQ
WAIS-III	Wechsler Adult Intelligence Scale, Third edition
WASI	Wechsler's Abbreviated Scale of Intelligence
WHO	World Health Organization

1. INTRODUCTION

Suicidal behaviour must be regarded as a disturbance of the fundamental striving to live, inherent in all living creatures, signifying that the individual's ability to cope has been exceeded (Nordentoft, 2007). Suicide is a tragic end to an individual's life, and a devastating loss to family and friends. Losing a patient to suicide is probably the worst fear of clinicians. Suicidal behaviour is a complex phenomenon with numerous influences, including the individual's psychology, biology, culture, social and political environment (McKenzie, Serfaty, & Crawford, 2003). Patients with psychotic disorders have a high prevalence of suicidal behaviour (Radomsky, Haas, Mann, & Sweeney, 1999), and the suicide rate is markedly elevated compared to the general population (Saha, Chant, & McGrath, 2007). Bleuler (1911) noted that the most serious of all schizophrenia symptoms was the suicidal drive, demonstrating that the high risk for suicidal behaviour was acknowledged even among the earliest researchers of schizophrenia. Several variables that increase the risk for suicidal behaviour in psychotic disorders have been identified (Hawton, Sutton, Haw, Sinclair, & Deeks, 2005a), but the reason for the elevated suicide risk is still not fully understood. Consequently, suicide-preventing strategies are incomplete, and acquiring more knowledge about phenomena related to suicidal behaviour in patients with psychotic disorders is imperative. The overall aim of the present thesis was to identify possible risk factors for suicidal behaviour in patients with psychotic disorders, with a special emphasise on patients with a first episode of psychosis.

1.1. Psychotic disorders

1.1.1. Definitions and classifications

The definition of the term *psychosis* has varied across history and is still used inconsistently. The narrowest definition of psychosis is restricted to a break in reality testing with distortion of perception (hallucinations) or thinking (delusions) with no insight into the pathological nature of these phenomena. Less restrictive definitions will include hallucinations that the individual realises are pathological, and even broader definitions will include other symptoms like disorganized speech and grossly disorganised or catatonic behaviour; symptoms seen in schizophrenia. The different psychotic disorders in the Diagnostic and Statistical Manual of

Mental Disorders (DSM-IV) emphasise different aspects of the diverse definitions (American Psychiatric Association, 1994).

The contemporary classification of psychotic disorders has its origin in Kraepelin's (1899) distinction between organic and functional psychoses, with the latter category separated into manic-depressive insanity and dementia praecox (later named bipolar disorder and schizophrenia, respectively). Although Kraepelin himself later came to question the dichotomous classification (Kraepelin, 1920), this view has dominated later work; bipolar disorder and schizophrenia have largely been viewed as discrete diseases (Crow, 1986) and are coded as such in the ICD-10 Classification of Mental and Behavioural Disorders (WHO, 1993) and DSM-IV (American Psychiatric Association, 1994). However, due to overlapping symptomatology, the dichotomous classification has been challenged over the last decades (Craddock & Owen, 2007). In addition, recent studies have found support for a common genetic base for schizophrenia and bipolar disorder (Craddock, O'Donovan, & Owen, 2009; Lichtenstein et al., 2009). Because of this, it has been suggested that the dichotomous stance should be departed, and an alternative view is that functional psychoses should be viewed along a continuum of symptoms. This debate is not yet resolved (Craddock et al., 2009), but studies across the functional psychosis continuum are encouraged in order to gain knowledge on the mechanisms of psychotic disorders (Ivleva, Thaker, & Tamminga, 2008).

In this thesis, the term *psychotic disorders* will include non-organic disorders classified as *Schizophrenia and other psychotic disorders* in the DSM-IV (American Psychiatric Association, 1994), i.e. disorders with psychotic symptoms as their defining features. Furthermore, psychotic disorders will include disorders classified as *Mood disorders* with psychotic symptoms in DSM-IV, in which disturbance of mood is the predominant feature, but where psychotic symptoms are also present. The different psychotic disorders are distinguished based on differences in duration, dysfunction, associated substance use, bizarreness of delusions, and presence of depression or mania (van Os & Kapur, 2009).

1.1.2. Schizophrenia

Schizophrenia is the most prevalent and the most studied of the psychotic disorders. It is found universally and in all cultures (Patel, Pinals, & Breier, 2008). Schizophrenia has a

relatively low median incidence rate of approximately 15 per 100 000 persons annually. Contrary to previously held assumptions that the rate of schizophrenia is consistent across the world, recent review studies have shown that incidence rates vary, with higher rates associated with male gender, urbanicity, and migration. The prevalence of schizophrenia also varies, with a median lifetime risk of developing schizophrenia of approximately 7 per 1000 persons. Higher prevalence is found in migrants compared to native-born individuals, and in developed versus developing countries (McGrath, Saha, Chant, & Welham, 2008). In comparison, one study focused on the broader range of psychotic disorders and found that the lifetime prevalence of schizophrenia was nearly 1%, raising to almost 4% when the broader range of psychotic disorders were included (Perala et al., 2007). The specific aetiology of schizophrenia remains unknown, but the leading view is that several factors interact to cause the illness. The basis for schizophrenia is an underlying psychobiological vulnerability, determined by genetic and environmental factors. The genetic component is strong, with heritability estimates of 80%. The incidence and expression of schizophrenia is determined by an interplay of biological and psychosocial factors (van Os & Kapur, 2009).

Patients with schizophrenia constitute a heterogeneous group. Schizophrenia is characterised by a variety of symptoms and signs, and several possible combinations of these may meet the diagnostic criteria. Central symptoms of schizophrenia include psychotic symptoms like hallucinations and delusions, also called positive symptoms, as they reflect an excess or distortion of normal functions. Another main group of symptoms are the negative symptoms, reflecting a reduction or loss of normal functions, such as affective flattening, impoverished thinking and speech, and lack of initiative (American Psychiatric Association, 1994). Although not a diagnostic criterion, neurocognitive impairment is highly prevalent in patients with schizophrenia (Keefe, Eesley, & Poe, 2005), and impairments are found in several neurocognitive domains (Tandon, Nasrallah, & Keshavan, 2009). Cognitive dysfunctioning is a strong predictor of poor social and vocational outcome (Green, Kern, & Heaton, 2004), which is also a defining criterion of the schizophrenia in the DSM-IV (American Psychiatric Association, 1994). As noted above, the psychotic disorders have overlapping symptomatology, but the features that typically distinguish schizophrenia from the other psychotic disorders are long duration, bizarre delusions, negative symptoms, and few affective symptoms (van Os & Kapur, 2009).

The onset of schizophrenia is usually in early adulthood; from the late teens to the mid 30's, although earlier and later onset also occur (American Psychiatric Association, 1994). The course of the disorder is heterogeneous; positive psychotic symptoms tend to be episodic over time, with varying degree and duration of remission in between. Negative symptoms and cognitive impairments tend to be more stable over time, and can still persist in phases when psychotic symptoms are less prominent (Tandon et al., 2009). Treatment of schizophrenia typically includes antipsychotic medication and psychosocial treatment. Schizophrenia is the most disabling of the mental disorders and causes considerable suffering. Worldwide, schizophrenia is among the ten leading causes of disability, requiring a disproportionate share of mental health services compared to its prevalence (Mueser & McGurk, 2004). The traditional clinical and public view is that schizophrenia is a debilitating and deteriorating disorder with poor outcome (van Os & Kapur, 2009). However, the prognosis of schizophrenia is heterogeneous; the disorder can develop into a severe state of defect, or end in varying degrees of partial or full recovery (Tandon et al., 2009). Most patients need some degree of support, but a majority live outside of hospitals, and hospital admissions are typically short (van Os & Kapur, 2009). Still, schizophrenia is associated with a variety of serious negative outcomes, including high unemployment rates (Rosenheck et al., 2006), poor quality of life (Eack & Newhill, 2007), and high prevalence of comorbid mental disorders, including depression, substance use, and anxiety disorders (Buckley, Miller, Lehrer, & Castle, 2009). Furthermore, schizophrenia is associated with increased mortality (Seeman, 2007), related to the high frequency of comorbid physical illness (Leucht, Burkard, Henderson, Maj, & Sartorius, 2007) and high risk of suicide (Palmer, Pankratz, & Bostwick, 2005).

1.1.3. First episode psychosis

Schizophrenia and related disorders develop through stages or phases, and the early stages include the premorbid phase, a prodromal phase, and the first episode of psychosis (FEP). While the prodromal phase is characterised by attenuated positive symptoms and declining function, the first episode of psychosis manifests fully fledged psychotic symptoms and marks the formal onset of the psychotic disorder (McGorry, Killackey, & Yung, 2007; Tandon et al., 2009). In samples of patients with FEP, schizophrenia spectrum disorders constitute approximately one third of the cases (Baldwin et al., 2005; Kirkbride et al., 2006). However, of note is the significant degree of diagnostic instability in this population (Baldwin et al.,

2005; Haahr et al., 2008). Although several studies of FEP-patients include only patients with schizophrenia or schizophrenia spectrum disorders, the diagnostic instability is the reason for recommendations to include the whole range of psychotic disorders, including psychotic affective disorders, when studying FEP-patients (Baldwin et al., 2005).

During the past 15 – 20 years, there has been a growing focus worldwide on identification and treatment of patients in the early phases of psychosis. These efforts were initially based on findings suggesting that early treatment and shorter duration of psychosis was related to better short-term (Falloon, 1992; Loebel et al., 1992) and long-term (Helgason, 1990) outcome. The first episode of psychosis can be divided into the period before and after treatment initiation. Studies have shown that that the period from onset of psychotic symptoms to the start of treatment, i.e. the period of untreated psychosis, can be disturbingly long. In patients with schizophrenia, the average mean duration of untreated psychosis (DUP) across different studies is between 1 – 2 years, and the median DUP at about 6 months (McGlashan, 1999). Thus, the goal in early psychosis intervention has been to minimise the DUP (McGorry et al., 2007). Studies have shown that this is possible; e.g. Melle et al. (2004) found that FEP-patients from an area where an early detection programme had been introduced had significantly shorter DUP than patients from an area without the early detection programme.

The notion of a possible causal relationship between DUP and outcome has been controversial because of inconsistent findings, and due to arguments that the relationship is confounded by variables such as poor premorbid functioning or insidious illness onset, which could both cause delayed treatment and are associated with poor prognosis (Perkins, Gu, Boteva, & Lieberman, 2005). However, two comprehensive meta-analytic studies found that DUP was related to a range of outcome variables, including symptomatic and functional recovery. The effect of DUP was independent of confounders, and prolonged DUP had a negative effect on recovery (Marshall et al., 2005; Perkins et al., 2005). Implementing health services to reduce the DUP has also shown promising results on outcome. Patients in areas with early detection programmes, coming to treatment with shorter DUP, had significantly lower symptom levels than patients outside of the early detection areas, both at study entry and at two-year follow-up (Melle et al., 2008).

Despite the above mentioned findings of the negative effects of prolonged DUP and findings of interventions to shorten the DUP, studies indicate that the DUP continues to be long; One meta-study reported a mean DUP of 103 week in several studies of FEP-patients (Marshall et al., 2005).

1.2. Suicidality

1.2.1. Terminology

Suicidality may be an all-inclusive term that includes suicidal thoughts, ideation, plans, suicide attempts and completed suicide. However, the definition of this term varies, exemplifying the conceptual debate surrounding suicidal phenomena (Silverman, 2006). In fact, one of the major difficulties in assessing, treating and preventing suicide is the lack of a consistent classification and operational definitions of suicidal behaviour (Maris, 2002). Neither the ICD-10 (WHO, 1993) nor in the DSM-IV (American Psychiatric Association, 1994) have definitions of suicidal behaviour, although ICD-10 lists suicidal acts in the E-codes (external cases of injury), and DSM-IV mentions suicidal behaviour as symptoms of depression and borderline personality disorder. For more than 50 years, researchers have tried to find satisfactory terms for the range of suicidal behaviours (Skegg, 2005), but the field is still characterised by unresolved challenges and controversy (Silverman, 2006). The present studies focused on suicidal ideation, including suicidal thoughts and suicidal plans, and suicide attempts. For the purpose of this thesis, only central concepts will be described.

The continuum of suicide ranges from suicidal ideas to gestures, risky lifestyles, suicidal plans, suicidal attempts, and finally completed suicide (Maris, 2002). Suicidal behaviour can be considered along two correlating dimensions; *intent* and *lethality* (Mann, 2002). Suicidal intent has been defined as the subjective expectation and desire for a self-destructive act to end in death (American Psychiatric Association, 2003), while lethality refers to the degree of damage resulting from a suicidal act (Mann, 2002).

Definitions of *suicide* vary according to theoretical orientation, but four key aspects have been identified as inherent in the definitions: 1) outcome (death), 2) agency of the act (self-inflicted), 3) intention to die, and 4) awareness of the outcome (Silverman, 2006); e.g. suicide

has been defined as self-inflicted death with explicit or implicit evidence that the person intended to die (American Psychiatric Association, 2003).

Non-fatal suicidal acts are described by several partly overlapping concepts (Skegg, 2005). The term *suicide attempt* has been defined as self-injurious behaviour with non-fatal outcome accompanied by explicit or implicit evidence that the person intended to die (American Psychiatric Association, 2003). Although definitions of attempted suicide also vary, they usually include reference to self-injurious behaviour with the intent to die. Alternative terms like *parasuicide* and *deliberate self-harm (DSH)* are generally applied to self-injurious behaviour regardless of the presence of suicidal intent. Hence, these terms are more heterogeneous and include a wider range of behaviour than suicide attempt (Silverman, 2006). In the present studies, we have focused on suicide attempts rather than DSH or parasuicide as suicide attempt is a more specific concept.

Suicidal ideation indicates no suicidal acts, and has been defined as thoughts of serving as the agent of one's own death. Suicidal ideation may vary in seriousness depending on the specificity of suicidal plans and degree of suicidal intent (American Psychiatric Association, 2003), indicating that suicidal ideation includes thoughts with or without a suicidal plan. S*uicidal plan* is a frequently used but rarely defined concept. However, it is often equated to having a suicide method (McKeon, 2009).

1.2.2. Prevalence of suicidal behaviour

Suicide is considered a significant public health problem. Self-inflicted death accounts for 1.5% of all deaths, and suicide is the tenth leading cause of death worldwide (Levi et al., 2003). The "global" annual suicide rate is 16 per 100 000 persons, and suicide is the third leading cause of death in the 15 – 44 year age group in some countries (WHO, 2010). In general, difficulties in discriminating suicides from accidental deaths probably cause official suicide rates to underestimate actual suicide rates (Nordentoft, 2007).

Suicide rates vary considerably between regions and countries. The lowest annual rates are reported in Latin America and Muslim countries, with fewer than 6.5 suicides per 100 000 persons. The highest rates are registered in Eastern Europe, where several countries report

more than 27 suicides per 100 000 per year (Mann et al., 2005). The UK and USA have suicide rates in the mid-range with rates per 100 000 of 12 for men and 3 for women in the UK, and 18 and 4 respectively in the USA (McKenzie et al., 2003). Within Europe, rates are generally higher in the north compared to the south, but countries at the same latitude can have very different rates (Hawton & Van Heeringen, 2009). In the Nordic countries, there are small differences between Norway, Iceland, Sweden and Denmark, with suicide rates of 12 – 14 per 100 000. Finland, however, have a much higher rate of 24 per 100 000 (Norwegian Institute of Public Health, 2009).

Comparison of suicide rates across different countries should be approached with caution. Countries differ in their death certification practices, and in requirements for a death to be recorded as a suicide. In some countries, suicide is illegal, which may probably affect registration practices. And in some parts of the world, epidemiological data on suicide is scarce (Hawton & Van Heeringen, 2009). However, differences in suicide rates between countries are not merely the result of registration biases; several studies show that suicide rates in immigrants tend to be more similar to rates in their native country than to rates in their current country of residence (Burvill, 1998; Malenfant, 2004), indicating that culture and ethnicity influence on suicide rates (Mann, 2002). In addition to regional differences, clear ethnic patterns in suicide rates are demonstrated. For instance, Native Americans have more than 50% higher suicide rates than European Americans, who have much higher suicide rates than Hispanic and African Americans (McKenzie et al., 2003).

Suicide rates also differ across time, age and gender. The rates are highest in elderly people in most countries, but over the past 50 years, rates have risen in the young, particularly in men (Wasserman, Cheng, & Jiang, 2005), and decreased in elderly people (Pritchard & Hansen, 2005). In Norway, suicide rates increased from the end of the 1960's to the end of the 1980's, followed by a 25% decrease in the suicide rate between 1988 and 1994. From 1994 the suicide rates have been relatively stable with a mean level of 12 pr 100 000 per persons annually, with no significant differences between persons over the age of 20 (Norwegian Institute of Public Health, 2009). In most regions of the world, men complete suicide more often than women do. The ratio of men to women is between two and four to one (Hawton & Van Heeringen, 2009). Attempted suicide is, however, more prevalent among women than

men worldwide, with few exceptions (Kerkhof, 2000). This could reflect the tendency for men to choose more lethal methods (e.g. hanging, shooting), while women tend to choose less violent means (e.g. self-poisoning) (Denning, Conwell, King, & Cox, 2000).

While many countries monitor deaths by suicide, no national or international surveillance system exists for monitoring the occurrence of suicide attempts (Silverman, Berman, Sanddal, O'carroll, & Joiner, 2007). However, non-fatal suicidal behaviours are believed to occur at a far higher rate than completed suicide; it is estimated that there are 10 – 25 non-fatal suicide attempts for every completed suicide (Maris, 2002). Suicidal ideation without action is even more common than suicidal acts (Mann, 2002). For instance, nearly 15% of American youths reported having seriously considered suicide within the previous year, and 40% of adults with depression wanted to kill themselves during their worst or most recent depressive episode (McKeon, 2009).

1.2.3. The development from suicidal ideation to suicidal acts

There is little research to describe how processes develop from suicidal ideation to actual suicidal acts (Silverman et al., 2007). Not surprisingly, however, research indicates that in general, different suicidal expressions are related to each other. Studies show that suicidal thoughts are related to increased risk for making suicide attempts (Kuo, Gallo, & Tien, 2001), and the risk for attempting suicide is significantly higher among individuals with a suicidal plan compared to individuals with suicidal thoughts (Borges et al., 2006; Kessler, Borges, & Walters, 1999). Furthermore, previous self-harm and suicide attempts increase the risk for later attempts. In prospective studies, between 0.5% and 2% of people who self-harm die by suicide within the first year, and more than 5% died within nine years (Owens, Horrocks, & House, 2002), with increased risk for individuals who repeated self-harm (Zahl & Hawton, 2004). One study of individuals who had made serious suicide attempts found a suicide rate of almost 7% after five years, while more than 37% had made at least one additional non-fatal suicide attempt (Beautrais, 2004). In most studies, a history of self-harm or suicide attempts is the strongest risk factor for death by suicide, present in approximately 40% of individuals who die by suicide (Cavanagh, Carson, Sharpe, & Lawrie, 2003; Hawton & Van Heeringen, 2009).

1.2.4. Suicidality and psychiatric illness

Suicide is strongly associated with psychiatric illness. Studies, mainly from Europe and North America, show that more than 90% of individuals who complete suicide have a mental disorder at the time of death (Bertolote, Fleischmann, De, & Wasserman, 2004; Cavanagh et al., 2003). Mood disorders are most commonly associated with suicide, followed by substance use-related disorders, schizophrenia, and personality disorders (Bertolote et al., 2004). Comorbidity of disorders increases the suicide risk.

More than half of the individuals who complete suicide have a current depressive disorder (Cavanagh et al., 2003). Approximately 4% of all depressed individuals die by suicide (Coryell & Young, 2005), and the risk is higher in patients hospitalised with depression (Bostwick & Pankratz, 2000). The risk is highest in the first episode of depression, possibly related to alcohol misuse, impulsivity, and aggressiveness, which seem to affect suicide in children and adolescents (McGirr et al., 2008). Risk factors associated with suicide in patients with major depression are high levels of hopelessness, high overall levels of suicidal tendencies, and history of attempted suicide (Coryell & Young, 2005).

Of patients with bipolar disorder, 10 – 15% die bye suicide, most often early in the illness course (Hawton & Van Heeringen, 2009). As with depressive disorder, the main risk factors related to suicide in bipolar disorder are previous suicide attempts and feelings of hopelessness (Hawton, Sutton, Haw, Sinclair, & Harriss, 2005b).

Substance misuse, and especially alcohol, is also strongly associated with suicide risk. A review of research showed that on average, 40% of suicide attempters and 37% of individuals who died by suicide had acute alcohol use (Cherpitel, Borges, & Wilcox, 2004). The suicide risk increases with severity of alcohol misuse, and thus the risk is higher for alcohol dependency than alcohol abuse, with an estimated suicide risk of 7% for patients with alcohol dependency. Predisposing factors for suicide related to alcohol dependency seem to be aggression, impulsivity, and hopelessness, while depression and stressful life events are key precipitating factors (Conner & Duberstein, 2004). Far more research has focused on alcohol than any other drug in relation to suicidal behaviour (McKeon, 2009). However, a variety of

other drugs have also been shown to be present at the time of suicide (Karch, Barker, & Strine, 2006).

Approximately 30 – 40% of all suicides are completed by individuals with a personality disorder, with an increased risk for borderline and antisocial personality disorders (Duberstein & Conwell, 1997), characterised by emotional lability, aggression, and impulsivity (Mann, 2002). However, most suicide completers with personality disorders have coexisting depressive symptoms, substance misuse, or both (Hawton & Van Heeringen, 2009).

Finally, the risk for suicide is also high in patients with schizophrenia (Palmer et al., 2005), and suicidality in psychotic disorders is the focus of the next chapter.

1.3. Suicidality in psychotic disorders

1.3.1. Prevalence of suicidal behaviour in psychotic disorders

The high frequency of suicidal attempts and completed suicide in patients with schizophrenia is well established. Studies also show that suicidal behaviour is prevalent in other psychotic disorders (Radomsky et al., 1999). There is a large literature on suicidality in affective disorders (i.e. depressive disorder and bipolar disorder), but few studies have specifically addressed psychotic affective disorders. Taken as a whole, most research on suicidality in psychotic disorders has focused on schizophrenia.

Suicide is the single leading cause of premature death among patients with schizophrenia (Brown, 1997), who have 12 times the risk of dying by suicide compared to the general population (Saha et al., 2007). Estimates indicate that 5 - 13 % of patients with schizophrenia will kill themselves (Caldwell & Gottesman, 1990; Palmer et al., 2005). These estimates vary due to different methodology; the 13% risk is an estimate of *proportionate mortality*, i.e. the percentage of the dead who died by suicide, while the 5% risk reflects *case fatality*, i.e. the percentage of the original sample who died by suicide. Proportionate mortality provides information only about the subjects in a study who are dead, but no information about subjects who are still alive. The use of proportionate mortality estimates poses a particular problem in schizophrenia and other psychotic disorders, because these disorders often have an

early age of onset (American Psychiatric Association, 1994), and the risk for suicide is highest in the early phases of illness (Palmer et al., 2005). The subjects who have survived the initial period of increased risk, have not yet entered the period of elevated risk of death from other causes. Thus, proportionate mortality assumes a constant suicide risk over the lifetime and will overestimate the suicide risk. As case fatality rates look at number of suicides as a fraction of the total sample, these rates are considered more accurate estimates of suicide prevalence than proportionate mortality. Accordingly, the lifetime risk for suicide in patients with schizophrenia is considered to be approximately 5% (Palmer et al., 2005). The prevalence of non-fatal suicidal behaviour is much higher; suicidal ideation and suicide attempts occur in as many as 50% of the patients with schizophrenia (Bolton, Gooding, Kapur, Barrowclough, & Tarrier, 2007).

1.3.2. Non-fatal suicidal behaviour

Suicidal symptoms are an additional burden for patients struggling with psychotic and related symptoms. In addition, suicidal ideation and suicide attempts are most likely distressing for relatives and health personnel. The study of non-fatal suicidal behaviour is thus important in its own right. However, the most important goal in studying suicidality is to prevent individuals from completing suicide. Despite this, we have focused on non-fatal suicidal behaviour in the present studies, i.e. suicidal ideation and suicide attempts. The reason for this is that psychotic disorders are infrequent, and even though patients with psychotic disorders have an increased suicide risk, completed suicide is relatively rare. To study completed suicide would involve recruitment of numbers of participants so large that it is practically impossible (Meltzer et al., 2003). Alternatively, completed suicide can be investigated in psychological autopsy studies, retrospectively collecting all available information about persons who died by suicide. This method, however, has some serious methodological challenges regarding the amount and accuracy of available data (Hawton et al., 1998). Consequently, the study of non-fatal suicidal behaviour as a proxy for completed suicide is widespread. In favour of this approach is the view that suicidal ideation and plans are important steps in a process that could lead to suicide attempts and possibly death (Kontaxakis et al., 2004). There are also studies supporting a relationship between different suicidal expressions in patients with psychotic disorders. Suicidal ideation has been associated with increased risk of suicide attempts (Harkavy-Friedman et al., 1999; Nordentoft et al.,

2002) and completed suicide, and attempted suicide is a strong predictor of later attempts and completed suicide (Hawton et al., 2005a). This indicates that suicidal phenomena of lower severity may serve as early warnings for more severe suicidality (Fialko et al., 2006).

1.3.3. Risk factors for suicidal behaviour in psychotic disorders

A number of different theoretical models of suicide in general has been suggested (Bolton et al., 2007). However, it has been argued that all models of suicidal behaviour in the end have to answer the question regarding which variables contribute to long term vulnerability (trait factors), and which represent short-term precipitating factors (state factors). As it turns out, some variables related to suicidality can be both trait- and state dependent (Williams, Crane, Barnhofer, & Duggan, 2005). Furthermore, it is unclear whether all variables related to increased risk in the general population also constitute a risk for patients with psychotic disorders (McGirr & Turecki, 2008). Still, identifying risk factors for suicidal behaviour is an important approach in the effort to predict and prevent suicide (Pompili et al., 2007).

A large body of research has identified variables that increase the risk for suicidal behaviour, and the following apply both to the general population (Hawton & Van Heeringen, 2009; Maris, 2002) and to patients with psychotic disorders. The most consistent demographical risk factors are being white and male (Hawton et al., 2005a; Montross, Zisook, & Kasckow, 2005), although the gender differences are less in schizophrenia than in the general population (Harkavy-Friedman & Nelson, 1997). The most important clinical risk factor is previous attempted suicide, significantly increasing the risk for later completed suicide. Greater lethality of the attempt and fewer measures taken for being rescued are also indicative of strong intent. Other major clinical risk factors are depression, both history of depression and recent depression, and feelings of hopelessness. The presence of drug misuse or -dependency also significantly increases the suicide risk (Hawton et al., 2005a; Montross et al., 2005). In view of the strong relationship between alcohol use and suicide in the general population, it is surprising to find that this relationship has been inconsistently reported in patients with psychotic disorders (Hawton et al., 2005a; Pompili et al., 2007). However, lack of social support is frequently noted as a risk factor (Montross et al., 2005) in both populations.

While the above mentioned risk factors are also found in the general population, some risk factors seem to be specific to psychotic disorders. Suicides happen at a younger age in patients with schizophrenia compared to the general population, with the highest risk occurring in the age range 22 – 40 years (Montross et al., 2005). This is consistent with the higher suicide risk early in the course of the disorder (McGirr & Turecki, 2008; Palmer et al., 2005). Patients with more severe illness courses have an increased risk for suicide; i.e. patients with more frequent and longer hospitalisations, more relapses and/or higher doses of antipsychotic medication. Patients with schizophrenia also have a higher risk for suicide within the first few weeks or months after discharge from hospital, which could be due to post-psychotic depression (Montross et al., 2005). It is also found that poor adherence to treatment, both medical treatment and attending follow-up, has been related to considerable increased suicide rate (Hawton et al., 2005a). Some studies find that the presence of active psychotic illness is related to suicide (Heila et al., 1997; McGirr et al., 2006; Westermeyer, Harrow, & Marengo, 1991), while reviews report of heterogeneous findings and a non-relationship between active illness and suicide. The relationship between suicide and specific positive symptoms like delusions and hallucinations has also been studied, but again with inconsistent findings (Hawton et al., 2005a; Montross et al., 2005). A few studies report of patients who have attempted suicide (Harkavy-Friedman et al., 2003) or completed suicide (Zisook, Byrd, Kuck, & Jeste, 1995) as a result of command hallucinations, but this occurs rarely and seems to be the exception rather than the rule (Montross et al., 2005). In sum, the role of psychotic symptoms in relation to suicide seems unresolved. However, it has been indicated that assumed consequences of psychotic disorders, i.e. fear of mental disintegration, increase the risk for suicide (Hawton et al., 2005a).

The prevalence of suicide attempts is higher then the rate of completed suicide. This could indicate that risk factors for attempted suicide are not the same as for completed suicide (McGirr & Turecki, 2008). However, most reviews have focused on suicide rather then suicide attempts. One study has reviewed risk factors for DSH in patients with schizophrenia, that is, risk factors for any acts of deliberate self-poisoning or self-injury (Haw, Hawton, Sutton, Sinclair, & Deeks, 2005). This study found that DSH was associated with suicidal ideation, previous DSH, past depressive episodes, drug abuse or drug dependency, and high number of psychiatric admissions; much resembling the above-mentioned variables

frequently associated with completed suicide. However, differences in risk factors for attempted and completed suicide have also been indicated. In the general population and in other clinical populations, men complete suicide more often than women, while women make more suicide attempts than men do. In patients with schizophrenia, the suicide rate is also higher in men, but when it comes to suicide attempts, the gender ratio seem to be more evenly distributed (Harkavy-Friedman & Nelson, 1997). Furthermore, suicide completers with schizophrenia have been shown to differ from attempters in being more depressed, hopeless, and socially isolated (Drake, Gates, & Cotton, 1986). Hence, risk factors for attempted suicide do not seem fully consistent with risk factors for completed suicide.

In sum, several risk factors for suicidal behaviour in schizophrenia and related disorders have been identified. However, it has been argued that these are of limited value in clinical practise because they are common phenomena and thus characterise a large group of people, including patients not at risk for suicide (Bolton et al., 2007). It is possible that gaining more knowledge about variables explicitly related to suicidality in patients with psychotic disorders will facilitate the identification of patients who are at actual risk for engaging in suicidal behaviour.

1.3.4. Neurocognitive function and suicidality in psychotic disorders

Neurocognitive impairment is an important component of schizophrenia (Keefe & Fenton, 2007), existing independently of clinical symptoms (Keefe et al., 2006) and neuroleptic medication (Torrey, 2002). Neurocognitive dysfunctions are highly prevalent in this patient group, although to varying degrees (Keefe et al., 2005). Impairments are found throughout the course of the disorder, i.e. in individuals at risk for developing schizophrenia (Erlenmeyer-Kimling et al., 2000), in the premorbid phase (Woodberry, Giuliano, & Seidman, 2008), in first-episode schizophrenia (Bilder et al., 2000), and in chronic schizophrenia (Harvey et al., 1999). Patients with schizophrenia have shown to have impairments in a range of neurocognitive domains, including episodic memory, processing speed, verbal fluency, attention, and executive function and working memory. The impairments appear to be more severe and persistent in patients with schizophrenia compared to patients with affective disorders, but not qualitatively different (Tandon et al., 2009). The significance of neurocognitive dysfunction seems to be substantial; several studies have shown that

neurocognitive impairments are related to several global and specific functional outcomes, e.g. poor social and occupational outcome, contributing to difficulties in managing daily activities (Green et al., 2004).

Suicidality in schizophrenia has been associated with higher IQ (De Hert, McKenzie, & Peuskens, 2001; Fenton, 2000), but not consistently (Kim, Jayathilake, & Meltzer, 2003; Nangle et al., 2006; Potkin, Anand, Alphs, & Fleming, 2003). IQ is a measure of global cognitive function. Few studies have investigated the relationship between more specific neurocognitive domains and suicidal behaviour in schizophrenia, and with inconsistent findings. Potkin et al. (2003) did not find a relationship between any specific neurocognitive domains and suicidality. Kim et al. (2003) found that patients with a history of lifetime suicidality performed better than patients without lifetime suicidality on measures of psychomotor speed, attention, working memory verbal fluency, verbal memory, and executive function, but this difference was mediated by feelings of hopelessness. Finally, Nangle et al. (2006) found that suicide attempters had better functioning than non-attempters on sub-components of executive functioning (attention and verbal fluency). Executive function includes volition, planning, purposive action, and self-monitoring of behaviour (Green, Kern, Braff, & Mintz, 2000). As impairment in executive processes could result in failure to formulate, plan and choose goal-directed actions, Nangle et al. (2006) have suggested that better executive functioning could imply better abilities to plan and initiate suicidal acts.

Impulsivity has also been hypothesised to predispose for suicidal behaviour (Mann, Waternaux, Haas, & Malone, 1999). The conceptualization of impulsivity varies, but there is some agreement that the general features of impulsive behaviour include rapid, spontaneous, ill-planned, excessive, and potentially maladaptive conduct (Enticott & Ogloff, 2006). An association between increased *behavioural* impulsivity and suicidality has been indicated in patients with schizophrenia (De Hert et al., 2001). In addition, *personality* measures of impulsivity have been associated with increased suicidal risk in several psychiatric disorders (Brezo, Paris, & Turecki, 2006), including schizophrenia (Gut-Fayand et al., 2001), though not consistently (McGirr et al., 2006). Personality measures of impulsivity typically rely on self-reports of previous impulsive behaviour, e.g. the Barratt Impulsiveness Scale (Patton, Stanford, & Barratt, 1995). Unlike neuropsychological measures, self-reports have the

advantage of assessing impulsivity across various settings, and may include reports of impulsivity in real-life settings. However, self-report measures assume that aspects of impulsivity, both cognitive processes and behaviour, are conscious to the individual. Furthermore, social desirability may influence the responses. Another concern is whether impulsive individuals, who by definition may present impulsive and incorrect responses, will provide valid answers to questions that depend on complex retrieval and summary of behaviours (Enticott & Ogloff, 2006). Accordingly, it has been suggested that the use of neuropsychological measures of impulsivity could prove to be more sensitive (Mann et al., 1999) and objective (Enticott & Ogloff, 2006) than clinical measures.

The ability to inhibit inappropriate responses is a key component of executive function (Cheung, Mitsis, & Halperin, 2004), and dyscontrol of inhibition is suggested to be a possible underlying cause of impulsivity. Hence, neuropsychological measurements of impulsivity commonly involve paradigms in which inappropriate responses must be inhibited (Enticott & Ogloff, 2006). A recent study found a relationship between inhibitory dyscontrol and personality measured impulsivity in a non-clinical sample (Enticott, Ogloff, & Bradshaw, 2006). Furthermore, impaired inhibition has been related to suicidality in different samples, including samples of bipolar disorder and mixed psychiatric disorders (Dougherty et al., 2004; Horesh, 2001; Raust et al., 2007; Swann et al., 2005; Wu et al., 2009). To our knowledge, no studies of this relationship have focused solely on patients with schizophrenia.

A model of suicidal behaviour has been proposed in which the risk for suicidal acts is influenced by individual trait-like predispositions (Mann et al., 1999). As neurocognitive impairments in schizophrenia are considered to be relatively stable over time (Heaton et al., 2001), neurocognitive differences between suicide attempters and non-attempters could elucidate trait differences that predispose for suicidal acts. However, since impaired neurocognitive functioning has been related to current suicidal state, investigation of the relationship between lifetime suicide attempts and neurocognitive traits needs to consider the possible confounding effect of current suicidality (Bryan, 2007).

1.3.5. Early psychosis and risk for suicidality

The reason for the high prevalence of suicidal behaviour in patients with psychotic disorders could be the strain of having psychotic symptoms over time, and the negative outcomes of the disorders. In view of this, it is surprising that the risk for suicide is highest in the early phases of the disorder (Palmer et al., 2005). Most suicides occur within the first decade after illness onset, and approximately 50% take place within the first two years of the disorder (Montross et al., 2005).

Studies of psychotic disorders have typically focused on suicidality in relation to treatment start rather than the actual onset of psychosis. However, risk factors for suicidal behaviour like depression (Hawton et al., 2005a) and substance use (Verdoux et al., 2001) are prevalent before treatment start (Larsen et al., 2006; Romm et al., 2010), indicating that the time before treatment start could be a period of increased suicide risk. In fact, studies have found that 14 – 28% of patients with FEP have attempted suicide prior to first treatment for psychosis (Bertelsen et al., 2007; Robinson et al., 2009). In addition, it appears that patients with untreated psychosis have a higher risk for violent suicide attempts compared to treated patients (Nielssen & Large, 2009). The relevance of directing attention to the period before treatment start is also indicated in a study finding that FEP-patients from an area with an early detection programme, involving coming to treatment at an earlier phase of the disorder and with lower symptom levels, reported less severe suicidality than patients from areas without the detection programme (Melle et al., 2006).

A few studies have focused on suicidality explicitly in the period between psychosis onset and treatment start, i.e. during the period of untreated psychosis. Within this period, 7 – 11% of patients with a FEP attempted suicide (Clarke et al., 2006; Foley et al., 2008) or engaged in self-harm (Harvey et al., 2008). As noted above, the duration of untreated psychosis can be alarmingly long (McGlashan, 1999). Some studies find that longer DUP is associated with increased risk for suicidal behaviour (Altamura, Bassetti, Bignotti, Pioli, & Mundo, 2003; Clarke et al., 2006; Harvey et al., 2008), though not consistently (Bakst, Rabinowitz, & Bromet, 2009; Foley et al., 2008; Nordentoft et al., 2002; Preti, Meneghelli, Pisano, & Cocchi, 2009). There is some evidence that risk factors for suicidal behaviour vary across different phases of illness (Addington, Williams, Young, & Addington, 2004; Clarke et al.,

2006). The reason for the inconsistent association between DUP and suicidal behaviour could be that the studies measure suicidality in different time intervals. To investigate this issue, DUP and suicidality in patients with psychotic disorders should be compared across specifically defined periods.

1.3.6. Insight into psychosis

Insight in psychosis encompasses the patients' experience of their disorder. Traditionally, insight was viewed as a unitary concept and an all-or none phenomenon. More recently, insight is viewed as a multidimensional and continuous construct. David (1990) defined insight along three overlapping dimensions: the individual's recognition of having a mental illness, compliance with treatment, and ability to relabel unusual mental events as pathological. Poor insight, also called "lack of awareness", is considered a key feature of psychosis, and has by many been seen as the actual defining characteristic of psychotic disorders (McGorry & McConville, 1999). Studies report that as many as 50 – 80 % of patients with schizophrenia do not believe they have a disorder (Amador & Gorman, 1998). Poor insight is found in all psychotic disorders, and most pronounced in schizophrenia and bipolar disorder (Amador et al., 1994; Pini, Cassano, Dell'Osso, & Amador, 2001). However, lack of insight does not seem to be a static phenomenon. Although it may persist in some patients (Cuesta, Peralta, & Zarzuela, 2000), insight may also improve during treatment (Wiffen, Rabinowitz, Lex, & David, 2010).

Poor insight is one of the main causes of treatment non-adherence in patients with schizophrenia (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002), and is thus considered to be an important clinical variable. However, overall, insight has been found to have apparently contradictory associations with outcome. Higher insight has been associated with lower symptom levels (Mintz, Dobson, & Romney, 2003) and with better treatment adherence, social functioning (Olfson, Marcus, Wilk, & West, 2006), and better work performance (Lysaker, Bryson, & Bell, 2002). But in addition, higher insight has been associated with more depression (Mintz et al., 2003), hopelessness (Carroll, Pantelis, & Harvey, 2004), and lower quality of life (Hasson-Ohayon, Kravetz, Roe, David, & Weiser, 2006). Insight has also been related to suicidal behaviour, but again with inconsistent findings; several studies show that presence of insight increases the risk for suicidal behaviour (Foley et al., 2008; Robinson

et al., 2009), while other studies find that only some aspects of insight are related to increased risk (Amador et al., 1996; Crumlish et al., 2005; Schwartz & Smith, 2004). There are also studies that do not find a relationship between insight and suicidality (Hawton et al., 2005a; Restifo, Harkavy-Friedman, & Shrout, 2009), and studies that report a protective effect of insight (Bourgeois et al., 2004; Steblaj, Tavcar, & Dernovsek, 1999). One possible explanation for the apparently contradictory findings between insight and outcome is that the impact of insight into psychotic disorders depends on the meanings attached to the disorder (Lysaker, Roe, & Yanos, 2007), i.e. the patients beliefs about psychosis.

1.3.7. Beliefs about psychosis

While insight into psychosis involves acceptance of a personal illness, regardless of knowledge and facts about of the illness (David, 1990), beliefs about psychosis are cognitions about psychotic disorders (Linden & Godemann, 2007), for instance about causation, treatment options, and prognosis. In general, beliefs about psychotic disorders seem to be highly negative. Of the psychotic disorders, most studies have focused on schizophrenia, which appear to be among the most stigmatized of the mental disorders (Crisp, Gelder, Rix, Meltzer, & Rowlands, 2000). People with schizophrenia are considered unpredictable and dangerous, and they elicit uneasiness, uncertainty, and fear in other people. Pessimistic beliefs about the course of schizophrenia prevail. In addition, very negative views about pharmacological treatments for mental disorders are common (Angermeyer & Dietrich, 2006). Media may at least partly be responsible for the prevalent negative beliefs; media coverage of schizophrenia is often negatively laden, including common use of stigmatising descriptors and frequently linking schizophrenia to violent events without putting the risk of violence into perspective (Clement & Foster, 2008). It is believed that beliefs about illness shape the emotional responses to illness and health-related behaviour (Salmon, 2000). In keeping with this view, studies have shown that psychoeducation for schizophrenia and related illnesses, with the intent to enhance the patients' knowledge of their illness, is related to reduced relapse or readmission rates, and a positive effect on the patients' well being (Pekkala & Merinder, 2002). It is not unlikely that patients who receive a diagnosis of schizophrenia or a related disorder will be influenced by the existing negative beliefs about schizophrenia. Studies show that negative illness perceptions have been related to depression and post-psychotic depression, anxiety, and low self-esteem (Iqbal, Birchwood, Chadwick, &

Trower, 2000; Karatzias, Gumley, Power, & O'Grady, 2007; Watson et al., 2006). In addition, negative illness perceptions have been related to suicidality (Fialko et al., 2006).

1.3.8. Insight, beliefs about psychosis, and suicidality

It is possible that the impact of insight on suicidality depends upon the individual's beliefs about psychosis. For instance, if the patient believes that a psychotic disorder means a chronic condition with deteriorating mental state, and that aspirations no longer can be achieved, then insight could possibly lead to depression, hopelessness and suicidal behavior. However, if the patient does not believe that psychosis prevents chances for a satisfying life, insight may not lead to the same pessimism. In support of this, studies have found that beliefs about psychosis moderate the relationship between insight and other aspects of outcome; i.e. patients with high insight accompanied by stigmatizing beliefs about mental illness have less hope, lower self-esteem, lower quality of life and more depression compared to patients with high insight and fewer stigmatizing beliefs (Lysaker et al., 2007; Staring, Van der Gaag, Van den Berge, Duivenvoorden, & Mulder, 2009). So far, no studies have focused on insight and beliefs about psychosis in relation to suicidality. This relationship seems especially relevant to explore early in the course of psychotic disorders when the suicide risk is highest. Also, insight, negative beliefs, and suicidality have all been related to depression (Beck, 2005; Hawton et al., 2005a; Mintz et al., 2003), which is especially prevalent in this phase of psychotic disorders (Romm et al., 2010). Finally, beliefs about psychosis may be particularly relevant to study in patients who have recently been faced with the reality of having a psychotic disorder, as it is likely that they hold the same negative beliefs about psychosis observed in the general population.

2. AIMS OF THE THESIS

The overall aim of the present thesis was to identify possible risk factors for suicidal behaviour in patients with psychotic disorders. As the risk for suicidal behaviour is highest in the early phases of psychotic disorders, the thesis focuses primarily on patients with a first episode of psychosis.

The aim of the first study was to investigate whether lifetime suicide attempters had better global cognitive functioning (higher IQ), better executive functioning, or higher impulsivity (poorer inhibitory control) than non-attempters in patients with schizophrenia spectrum disorders. The possible confounding effect of current suicidality on the relationship between neurocognitive performance and lifetime suicide attempts was taken into account.

The aim of the second study was to explore the prevalence and characteristics of patients with a first episode of psychosis and suicidality in two different time intervals: 1) prior to study entry and 2) explicitly in the period of untreated psychosis. As previous attempted suicide is a strong predictor of later attempts and completed suicide (Hawton et al., 2005a), we focused particularly on suicide attempts in the two time intervals.

The aim of the third study was to explore the relationship between insight, beliefs about psychosis, depressive symptoms, and current suicidality in patients with first episode psychosis. In particular, we investigated whether a relationship between insight, negative beliefs about psychosis, and suicidality was mediated by depressive symptoms. Furthermore, we predicted that beliefs about psychosis would moderate the effect of insight on suicidality, i.e. we expected that higher insight would be associated with current suicidality in patients with negative beliefs about psychosis, but not in patients without negative beliefs about psychosis.

3. MATERIAL AND METHODS

3. 1. Setting

The present studies were part of the Thematically Organized Psychosis research (TOP) study, a large translational research study affiliated with the University of Oslo. The overall aim of the TOP study is to investigate clinical and biological characteristics of psychotic disorders in order to gain more knowledge about pathophysiological mechanisms. Patients included in the TOP study were recruited consecutively from in- and out patient psychiatric units in four hospitals in the Oslo region, covering a catchment area of 485 000 inhabitants, and Innlandet Hospital Trust, covering the neighbouring counties of Hedmark and Oppland, a catchment are of 374 500 inhabitants. Taken together, these catchment areas cover urban, suburban and rural areas. Mental health care in Norway is organized in catchment areas, offering public mental health care to all individuals within a given catchment area, and resulting in a high degree of patient representativity. Patient inclusion started in October 2002 and is still ongoing. The TOP study aims at including all patients with psychotic disorders in treatment at the cooperating hospitals, but the main diagnostic categories included in the TOP study are schizophrenia- and bipolar spectrum disorders. The TOP study collects clinical and neurocognitive data, data from structural and functional MRI, and genetic information. The present studies are based on clinical and neurocognitive data from the TOP study.

3.2. Design

The present studies are naturalistic, cross-sectional studies involving group comparisons.

3.3. Material

The present studies included an overall number of 398 patients with psychotic disorders. The samples in the three studies differed to some extent. This is partly due to the ongoing inclusion process and thus increasing number of patients included in the TOP study, but also due to different aims and methodology in the different studies (see table 1). Patients included in study I and II were recruited from the Oslo region, while study III also included patients from Innlandet Hospital Trust.

Table 1 Samples in study I, II, and III.

	N	Patient group	Inclusion period
Study I	174	Schizophrenia spectrum disorders	May 2003 - September 2007
Study II	170	First episode of psychosis	September 2004 - July 2008
Study III	194	First episode of psychosis	March 2006 - October 2009

Inclusion criteria specific for study I was a schizophrenia spectrum disorder according to the DSM-IV (American Psychiatric Association, 1994), i.e. schizophrenia, schizoaffective disorder or schizophreniform disorder. Furthermore, in order to assure valid neuropsychological test performance, all patients in study I had to have Norwegian as their first language or have received their compulsory schooling in Norway. Additionally, they had to have 14 or more correct responses on the forced recognition task on the California Verbal Learning Test, second edition (CVLT-II) (Delis, Kramer, Kaplan, & Ober, 2004), as proof of adequate test effort.

An inclusion criterion specific for study II and III was a first episode of a psychotic disorder according to the DSM-IV (American Psychiatric Association, 1994), including affective disorders with mood-incongruent psychotic symptoms, and excluding psychotic disorders due to general medical condition or substance use. Patients were considered to have a first episode of psychosis if they had not previously been treated with antipsychotic medication for more than 12 weeks or until remission. They were eligible for inclusion up to 52 weeks following the start of adequate treatment, defined as admission to hospital due to psychosis or antipsychotic medication in adequate dosage.

The inclusion criterion in common for all three studies was age 18 – 65 years. Exclusion criteria common for the three studies were history of severe head injury, brain damage, neurological disorder, and mental retardation.

There was some sample overlap between the three studies. Forty-two patients from study I were also included in study II, and 24 patients from study I were included in study III. Ninety-four patients from study II were also included in study III.

3.4. Methods

The TOP study protocol encompasses measurements of a range of demographic, clinical, and neuropsychological variables. Only assessments relevant for the present studies are presented in this thesis.

3.4.1. Clinical assessment

3.4.1.1. Diagnoses

Diagnoses were set according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), modules A-E (First, Spitzer, Gibbon, & Williams, 1995). All interviewers completed a training course in SCID-I assessment. In order to assure diagnostic inter-rater reliability, regular diagnostic consensus meetings were held. In addition, all interviewers received individual supervision by senior clinicians on diagnostic matters. Mean overall kappa for SCID-I diagnosis was 0.77. In order to assess reliability of diagnosis for actual study participants, a stratified random sample of cases from every interviewer was drawn, and clinical vignettes were rated by two experts blind to the study assessments. For 28 vignettes the overall agreement for DSM-IV diagnoses was 82% and the overall kappa 0.77 (95% CI: 0.60 – 0.94).

3.4.1.2. Symptoms and functioning

Psychotic and related symptoms the last seven days were rated on the Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987), based on information from the Structured Clinical interview for the Positive and Negative Syndrome Scale (SCI-PANSS) (Kay, 1991). The PANSS is a 30-item rating scale where each item is rated from 1 (“Absent) to 7 (“Extreme”). Symptoms were characterised on the PANSS positive subscale, negative subscale, and general psychopathology subscale. The inter-rater reliability for PANSS was adequate with intraclass coefficient (ICC) of 0.82 (95% CI: 0.66 – 0.94) for the positive subscale, 0.76 (95% CI: 0.58 – 0.92) for the negative subscale, and 0.73 (95% CI: 0.54 – 0.90) for the general psychopathology scale).

Insight was assessed by the PANSS item G12 (Lack of judgement and insight), and a lower score indicated more insight.

Current depression (last seven days) was assessed by PANSS item G6 (Depression) in study I. In study II and III, current depression (past two weeks) was measured by the Calgary Depression Scale for Schizophrenia (CDSS) (Addington, Addington, & Schissel, 1990), a 9-item rating scale where each item is rated from 0 ("Absent") to 3 ("Severe").

Global level of symptoms and functioning was measured by the Global Assessment of Functioning scale (GAF), split version with symptom scores assessed on the GAF symptom scale (GAF-S) (study I) and functioning assessed on the GAF functioning scale (GAF-F) (study I and III) (Pedersen, Hagtvet, & Karterud, 2007). Each scale is scored from 0 – 100, with higher scores indicating fewer symptoms/better functioning. ICC for GAF-S was 0.86 (95% CI: 0.77 – 0.92) and 0.85 (95% CI: 0.76 – 0.92) for GAF-F.

Premorbid functioning was measured with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor, Potkin, & Wyatt, 1982) (study I and II). The PAS is a rating scale that measures level of functioning in four age periods, scored from 0 (best level of functioning) to 6 (worst level of functioning). The scores were divided into two domains: academic and social. For each domain, childhood scores and scores of premorbid change (the difference between latest available score and childhood score) were calculated (Haahr et al., 2008). For childhood functioning, lower scores indicate better functioning. For change in functioning, positive scores indicated a decrease in premorbid functioning while negative change scores indicated an increase in premorbid functioning.

3.4.1.3. Suicidality

Suicidality was measured in different ways according to the different aims of the three studies. In study I, information on presence of lifetime suicide attempts were obtained in the SCID-I interview (First et al., 1995), which is based on all available information, including the patient' responses to the interview and information from medical records. Study I also measured current suicidality based on information from item 8 ("Suicide") on the CDSS (Addington et al., 1990) for 69 patients, and item 18 ("Suicidal thoughts") on the Inventory of Depressive Symptoms – Clinician rated (IDS-C) (Rush, Gullion, Basco, Jarrett, & Trivedi, 1996) for 131 patients. While the CDSS is based on symptomatology the last two weeks, IDS-C measures symptoms the last week. The IDS-C items are rated on a 0 – 3 point scale, with higher scores indicating more severe symptom levels. For the 26 patients who were

evaluated by both questionnaires, suicidality scores were congruent for 22 patients. In cases of incongruence, the score indicating presence of suicidality was chosen. The rate of concordant and disconcordant ratings of suicidality in CDSS and IDS-C correspond to a kappa value of 0.73.

In study II, suicidality was measured by asking the patients whether they had experienced suicidal thoughts, suicidal plans, or attempted suicide in three different time periods, i.e. before psychosis, during the period of untreated psychosis, and after treatment start. The merging of these time intervals constituted the time interval *prior to study entry*. Based on this information, patients were also categorised according to level of suicidality, i.e. non-suicidal, suicidal ideation (suicidal thoughts or suicidal plans), and suicide attempts.

In study III, current suicidality was measured by item 8 on the CDSS (Addington et al., 1990).

3.4.1.4. Illness course

Age at illness onset (study I) and psychosis onset (study II and III) were defined as age at first SCID-verified psychotic symptom. Duration of illness (study I) was defined as the difference between age at clinical interview and age at illness onset. Age at first depression (study II) was defined as age at first SCID-verified depressive symptom. Number of lifetime psychotic episodes and depressive episodes (study I and II) were registered based on the SCID-interview (First et al., 1995). The time between start of adequate treatment, as defined above, and clinical interview was registered in months (study III). In study II and III, DUP was measured in weeks from psychosis onset until start of adequate treatment, as defined above. Presence of psychosis was defined as a score of ≥ 4 on items P1 (Delusions) , P3 (Hallucinatory behaviour) , P5 (Grandiosity), P6 (Suspiciousness/persecution), or G9 (Unusual thought content) on the PANSS (Kay et al., 1987). All raters of DUP were trained in the general evaluation of DUP, which included consensus ratings of randomly drawn cases. Cases that were difficult to rate were evaluated under supervision of a senior psychiatrist with expertise in the first episode psychosis-field.

3.4.1.5. Demographical data, substance use, and medication

Information on demographical data, substance use, and medication were obtained from a detailed clinical interview and hospital records. This information included alcohol use

(number of alcohol units) and substance use (times used) during the six months prior to study entry. In addition, lifetime diagnoses of alcohol disorder or drug disorder were established in the SCID-I interview (First et al., 1995) (study II). Information about the use of medication at the time of neuropsychological testing was used in study I. Antipsychotic medication was classified as typical or atypical medication, and also calculated into chlorpromazine equivalents.

3.4.1.6. Beliefs about psychosis (Study III)

Beliefs about psychosis were measured by the self-report questionnaire Attitudes and Beliefs about Mental Health problems, schizophrenia version (Jorm, Korten, Jacomb, Christensen, & Henderson, 1999). The questionnaire was translated into Norwegian, translated back into English, and approved by the author (Appendix 1). The questionnaire is based on a vignette describing a person with symptoms fulfilling the ICD-10 (WHO, 1993) and DSM-IV (American Psychiatric Association, 1994) diagnostic criteria for schizophrenia. The patients had to answer several questions related to the person in the vignette, and the following information from the questionnaire was selected for study III: [a] recognition of the psychotic disorder (open question); [b] assumptions of prognosis if given professional help (rated on a six point scale where 1 = "full recovery with no further problems" and 6 = "get worse"); [c] assumptions of five negative long-term outcomes for the vignette-person compared to other people (scored "more likely", "just as likely", or "less likely". The responses were summed and the variable was dichotomised into "not more likely vs. more likely"); and finally [d] assumptions about discrimination occurring ("no"/"yes").

3.4.2. Neuropsychological assessment (study I)

The neuropsychological test battery was designed in order to include measures of a broad range of neurocognitive domains shown to be impaired in psychotic disorders (Bilder et al., 2000). Tests that were translated into Norwegian and easily applied in clinical settings were given priority over experimental paradigms not available for common use.

Current IQ was subdivided into verbal IQ (VIQ) and performance IQ (PIQ), measured by Wechsler's Abbreviated Scale of Intelligence (WASI) (Wechsler, 2007). VIQ is the sum of scores on the Vocabulary and Similarities sub items. The score on Vocabulary is the sum of

points achieved for explaining list of 42 words. The score on Similarities is the sum of points achieved for explaining what each of 26 pair of words has in common. PIQ is the sum of scores on Block Design and Matrix reasoning. The score on Block Design is points achieved constructing replicas of 13 block constructions made by the examiner and print designs. The score on Matrix Reasoning is points achieved from choosing from multiple-choice array the items that best complete 35 different visual patterns.

Premorbid IQ was estimated with the National Adult Reading Test (NART), based on errors in reading 50 phonetically irregular words, and adjustet for age years of education and age (NART premorbid IQ = 107.5 – [NART errors ×0.52] + [education × 1.16] – [age × 0.1]) (Sundet & Vaskinn, 2008).

Executive functioning was measured by the Color-Word Interference Test (C-W-Interference test) from the Delis Kaplan Executive Functioning Scale (D-KEFS) (Delis, Kaplan, & Kramer, 2005). Scores from condition 3 (Interference) were used, the score being time taken to name the colour of the ink on a list of written names of colours that are incongruent with the colour of the ink. Also included was condition 4 (Set-shifting), where the measure used was time taken to complete the alternation between naming the colour of the ink and naming the written word. In addition, from the Verbal Fluency Test (D-KEFS) (Delis et al., 2005), the third condition (Category switching) was used, where the score was the total number of fruit and furniture generated within 60 seconds while alternating between the two categories. Finally, executive function was measured by CVLT-II (Delis et al., 2004), where a list of 16 words is read five times, and the categorisations of words after the reading trials were measured. The scores were degree of recall according to semantic categories (Semantic cluster ratio), recall according to the order of words read (Serial-order cluster ratio), and degree of idiosyncratic recall (Subjective cluster ratio). Also measured was the average number of new words per trial acquired across the five reading trials (Learning slope), and the percentage of the same words recalled across the reading trials of the list (Recall consistency).

As impulsivity is suggested to arise from impairments in inhibition of inappropriate responses (Enticott & Ogloff, 2006), *inhibitory control* was measured by errors on condition 3

(Interference) and condition 4 (Set-shifting) on the C-W Interference Test (D-KEFS) (Delis et al., 2005).

Motor functioning was measured by Grooved Pegboard (Matthews & Kløve, 1964). The score was seconds to complete insertion of pegs into a board, averaged for both hands.

Psychomotor tempo measured by Digit Symbol on Wechsler Adult Intelligence Scale, Third edition (WAIS-III) (Wechsler, 2003). The score was number of correct digits filled in according to a key pairing symbol and digit within 120 seconds.

Attention was measured by the Digit Span Test (WAIS-III) (Wechsler, 2003). The total number of digits repeated in the same order as presented (forward and backwards) was scored.

Verbal memory was assessed by the Total list A 1 – 5 from the CVLT-II (Delis et al., 2004). The measure was the total number of words repeated immediately after five reading trials of a list of 16 words.

3.5. Procedures

Patients with a suspected or confirmed psychotic disorder were asked by their clinician in charge of treatment about participation in the TOP study. Interested patients were then referred to the study assessment team. Study assessment took place at the patients' treatment units or at the premises of the TOP study. For patients with a first episode of psychosis, the assessment was carried out as soon as possible after treatment start. The clinical assessment was conducted by psychiatrists or psychologists who had completed the training and reliability program in the TOP study. The clinical interview was carried out over the shortest period possible in order to avoid dispersion of symptom measures, but was divided into several appointments when required according to the patients' condition.

The neuropsychological assessment was conducted within 14 days of the clinical assessment and was conducted by psychologists with training in standardised neuropsychological testing. Test scoring was initially calibrated across the investigators in order to assure inter-rater

reliability, and the test-administrators were supervised by a specialist in neuropsychology. A report of the results from the clinical assessment and one from the neuropsychological assessment were sent to the treatment units with the patients' consent. The result of the assessments was also given in person to the patients and their treating clinicians.

3.6. Ethical considerations

The TOP study has been approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. All participants signed written informed consent. Participants received thorough information about the study aim, voluntary participation, the different assessments of the TOP study, confidentiality and security of data handling, and the right to withdraw from the study at any point in time. Patients with psychotic disorders may have cognitive impairments, and written information was thus supplemented by oral information when required.

The patients were approached at their treatment units about study participation. It was therefore emphasised that participation was voluntary and that refusal would not have consequences for their treatment. Patients did not get monetary compensation for their participation, with the exception of travelling expenses.

The TOP study has a comprehensive assessment protocol. Patients were approached at both inpatient and out patient units, reflecting different phases and severity of psychotic illness. Despite the comprehensive and time consuming assessment, the burden for the patients was considered not to exceed that of a thorough clinical examination. The assessment was carried out according to the patients' level of illness, i.e. over several appointments and with breaks when needed.

3.7. Statistical analyses

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) (SPSS Inc, Chicago, Il, USA) versions 15 and 16. Group comparisons of demographical, clinical, and neurocognitive variables were conducted with a range of analyses. All tests were 2-tailed, and level of significance was set at 0.05. Categorical variables were analysed with

Chi-square tests. For comparison of two groups, continuous variables that were normally distributed were analysed with Student t-tests, while skewed variables were analysed with Mann-Whitney U tests. For comparison of three groups, normally distributed continuous variables were analysed with one-way analyses of variance (one-way ANOVA) with post hoc Scheffe's tests, while skewed variables were analysed with Kruskal-Wallis tests and post hoc Mann U-Whitney tests. Exploration of interaction effects between two independent variables were conducted with two-way ANOVA. Correlations between variables were investigated with Pearson correlation or Spearman rank order correlation analyses, depending on type of variables. In order to control for possible confounding variables in study I, a series of hierarchical multiple regression analyses was used. The predictive value of variables was investigated with binary regression analyses in study II and III. Highly skewed variables were logarithm transformed for the regression analyses. Detailed descriptions of the statistical analyses used in the studies are presented in the three papers.

4. RESULTS/SUMMERY OF PAPERS

Paper I: Neurocognitive functioning and suicidality in schizophrenia spectrum disorders

Introduction: Suicidal behaviour and neurocognitive impairment are serious and prevalent problems in schizophrenia. Studies indicate that suicidality in schizophrenia may be associated with relatively higher neurocognitive functioning, but the findings are few and inconsistent. Also, behavioural- and personality measures of impulsivity have been linked to increased suicidal behaviour in schizophrenia, but this relationship has not been studied by neuropsychological measures. The aim of this study was to investigate whether suicide attempters had higher IQ, better executive functioning, or were more impulsive as measured by neuropsychological tests than non-attempters in a group of patients with schizophrenia spectrum disorders.

Method: One hundred seventy-four patients with schizophrenia spectrum disorders were assessed with a clinical interview for diagnosis, suicidality, symptoms and function, and underwent an extensive neurocognitive test battery.

Results: There were no statistically significant differences in any neurocognitive domains between lifetime suicide attempters and non-attempters, or between patients with different rates of suicide attempts. Currently suicidal patients were significantly more impulsive (had poorer inhibitory control) than currently non-suicidal patients, but this difference was mediated by positive psychotic symptoms.

Conclusion: The findings indicate that among patients with schizophrenia spectrum disorders, there are no significant differences in IQ or neurocognitive functioning between suicide attempters and non-attempters.

Paper II: Suicidality before and in the early phases of first episode psychosis

Introduction: The suicide risk in psychotic disorders is highest in the early phases of illness. Studies have typically focused on suicidality from treatment start rather than actual onset of psychosis. This study explored the prevalence and characteristics of suicidality in patients with a first episode of psychosis in two time intervals: 1) prior to study entry and 2) explicitly in the period of untreated psychosis.

Method: One hundred seventy FEP-patients were interviewed as soon as possible after treatment start. The interview included assessments of diagnoses, suicidality, symptoms, substance use, and premorbid functioning.

Results: Nearly 26% of the patients attempted suicide prior to study entry and 14% made suicide attempts during the period of untreated psychosis. Of the patients who had been suicidal (i.e. experienced suicidal ideation or attempts), 70% were suicidal during the period of untreated psychosis. Suicide attempts prior to study entry were associated with female gender, more depressive episodes, younger age at psychosis onset, and history of alcohol disorder. Suicide attempts during untreated psychosis were also associated with more depressive episodes and younger age at illness onset, in addition to drug use the last six months and longer duration of untreated psychosis.

Conclusion: The prevalence of suicidality before and in the early phases of FEP is high, especially during untreated psychosis. As prolonged DUP is associated with suicide attempts during the period of untreated psychosis, reducing the DUP could have the effect of reducing the prevalence of suicide attempts in patients with FEP.

Paper III: Suicidality in first episode psychosis is associated with insight and negative beliefs about psychosis

Introduction: Suicidal behaviour is prevalent in psychotic disorders. Insight has been found to be associated with increased risk for suicidal behaviour, but not consistently. A possible explanation for this is that insight has different consequences for patients depending on their beliefs about psychosis. The present study investigated whether a relationship between insight, negative beliefs about psychosis and suicidality was mediated by depressive symptoms, and if negative beliefs about psychosis moderated the relationship between insight and suicidality in patients with a first episode of psychosis.

Method: One hundred ninety-four FEP-patients were assessed with a clinical interview for diagnosis, symptoms, functioning, substance use, suicidality, insight, and beliefs about psychosis.

Results: Nearly 46% of the patients were currently suicidal. Depressive symptoms, having a schizophrenia spectrum disorder, insight, and beliefs about negative outcomes for psychosis were independently associated with current suicidality; contradicting a mediating effect of

depressive symptoms. Negative beliefs about psychosis did not moderate the effect of insight on current suicidality.

Conclusion: The results indicate that more depressive symptoms, higher insight, and negative beliefs about psychosis increase the risk for suicidality in FEP-patients. The findings imply that monitoring insight should be part of assessing the suicide risk in patients with FEP, and that treating depression and counteracting negative beliefs about psychosis may possibly reduce the risk for suicidality.

5. DISCUSSION

5.1. Discussion of main findings

5.1.1. Neurocognitive functioning and suicidality in schizophrenia spectrum disorders

In study I, we found that suicide attempters did not have higher IQ than non-attempters in a sample of patients with schizophrenia spectrum disorders. This finding is in keeping with other studies of *suicide attempts* (Potkin et al., 2003; Nangle et al., 2006), but inconsistent with studies finding an association between higher IQ and *completed suicide* (De Hert et al., 2001). However, as suicide attempts occur at a far higher rate then completed suicide, it is not unexpected that the predictors of attempts differ from predictors of suicide (McGirr & Turecki, 2008).

We also found that suicide attempters did not have better executive function compared to non-attempters, consistent with the findings of Potkin et al. (2003). This result contradicts a strong relationship between level of executive function and propensity to carry out suicidal acts. Our result is inconsistent with one other study finding a relationship between sub-components of executive function (attention and verbal fluency) and suicide attempts (Nangle et al., 2006). Executive function comprises of multiple processes (Kerns, Nuechterlein, Braver, & Barch, 2008), and it is possible that Nangle et al. (2006) used neuropsychological tests that measured executive processes that were more closely related to engagement in suicidal acts. Study I, however, included several different measurements of executive function, assessing different executive processes. If executive function did play an essential part of engaging in suicidal acts, we could expect this to come across in different test. Also, studies have indicated that poorer executive function is related to being currently suicidal (Marzuk, Hartwell, Leon, & Portera, 2005; Westheide et al., 2008). Nangle et al. (2006) did not control for the possible effect of current suicidality, and without this information, it is difficult to compare our results directly with theirs.

Study I is the first to examine neuropsychologically measured impulsivity in relation to suicidality in a sample consisting of only patients with schizophrenia spectrum disorders. We did not find suicide attempters to be more impulsive, i.e. to have poorer inhibitory control than non-attempters, indicating that impulsivity is not an essential part of attempting suicide

in patients with schizophrenia spectrum disorders. However, this result contradicts previous findings of a relationship between neuropsychologically measured impulsivity and suicide attempts in other populations (Dougherty et al., 2004; Raust et al., 2007; Swann et al., 2005; Wu et al., 2009). Again, it is possible that the tests used in the other studies measure processes that are more relevant for carrying out suicidal acts. Our result is also inconsistent with the findings of an association between personality measured impulsivity and suicidality in patients with schizophrenia (Gut-Fayand et al., 2001). A possible explanation of our finding is that impulsivity does not characterise all suicide attempters, but that impulsive patients constitutes a high risk subgroup (Horesh, 2001) whose impulsive features are masked by the group as a whole. One possible subgroup is repeaters of suicidal behaviour, who have shown to be more impulsive than non-repeaters (Evans, Platts, & Liebenau, 1996). This finding was not supported in study I; we did not find a difference in impulsivity between patients without suicide attempts, patients with a single attempt, and patients with multiple attempts. However, despite the reasonable large sample size, the group of patients with multiple attempts was small (n = 24), and lack of association with impulsivity may have been due to lack of statistical power.

Another possible explanation why our result contradicts studies of personality measured impulsivity is that measurements of inhibitory control may not be comparable to personality measures of impulsivity. This is as suggested by a recent study finding that non-psychotic suicide attempters were more impulsive than non-attempters on both personality measures and neuropsychological measures, but the measurements of impulsivity did not correlate (Wu et al., 2009). Although inhibitory paradigms are commonly used to study impulsivity, it is unclear which inhibitory paradigm is the one most closely related to impulsive behaviour, and whether inhibitory control underlies all impulsive behaviour (Enticott & Ogloff, 2006). It is also possible that impulsivity is not a unitary construct, but rather includes several components or dimensions that demand different measurements (Wu et al., 2009).

A final explanation of the discrepancy between our results and previous findings is that even though impulsivity has been considered to be a relatively stable trait, it could be less stable than initially thought (Gut-Fayand et al., 2001). In keeping with this view, it has been suggested that there is a distinction between having an impulsive cognitive style and making

impulsive suicide attempts, and that these dimensions do not overlap completely (Baca-Garcia et al., 2005).

The lack of difference between suicide attempters and non-attempters in IQ, executive functioning, and impulsivity was not confounded by group differences in demographical and clinical variables. Studies have found that impaired neurocognitive function has been associated with current suicidal state (LeGris & van Reekum, 2006; Marzuk et al., 2005; Westheide et al., 2008) and consequently, an investigation of the relationship between neurocognitive function and suicide attempts also needs to consider the possible confounding effect of current suicidal symptoms (Bryan, 2007). However, we found that the lack of relationship between neurocognitive function and lifetime suicide attempts was not confounded by differences in current suicidality.

A post hoc result of note in study I was that patients who were currently suicidal were more impulsive, i.e. had poorer inhibitory control, than patients who were currently non-suicidal, and this difference was mediated by differences in PANSS positive psychotic symptoms. The findings regarding presence of psychotic symptoms in relation to suicide have been inconsistent (Hawton et al., 2005a), but some studies report that active psychotic illness can be highly prevalent in the immediate time preceding suicide (Heila et al., 1997). If patients with current suicidality and higher levels of positive symptoms are more impulsive, this combination of symptoms could constitute an increased risk for suicidal acts. However, this finding was not based on an a priory hypothesis and should thus be interpreted with caution.

In sum, suicide attempters and non-attempters did not differ in IQ, executive function, impulsivity or any other neurocognitive domains measured in this study.

5.1.2. Suicidality before and in the early phases of first episode of psychosis

In study II, we found that suicidal behaviour was highly prevalent in patients with first episode psychosis. In the period prior to study entry, almost 39% of the patients had experienced suicidal ideation, while nearly 26% had attempted suicide. The prevalence of suicide attempts in the early phases of psychosis varies across different studies (Nielssen &

Large, 2009). Our result is in the higher range, but comparable to rates in similar samples (Nordentoft et al., 2002). The rates of suicidality confined to the period of untreated psychosis was also high; more than 31% of patients had experienced suicidal ideation, while over 14% had attempted suicide. This rate of suicide attempts is somewhat higher than rates found by others (10% and 7%) (Clarke et al., 2006; Foley et al., 2008). Of all the patients who had experienced suicidal ideation or attempted suicide before study entry, 70% had been suicidal during the period of untreated psychosis. In addition, of all the attempters, more than 54% had attempted suicide within the period of untreated psychosis. This underlines that suicidality is especially prevalent after the onset of psychosis and before treatment is initiated.

Suicide attempts made prior to study entry and specifically during untreated psychosis were associated with younger age at psychosis onset and more depressive episodes. While attempting suicide before study entry was specifically associated with female gender and a lifetime history of alcohol disorder, attempts made during untreated psychosis were associated with the use of drugs the last six months prior to study entry. The most important difference between attempting suicide prior to study entry and during the period of untreated psychosis was that only suicide attempts made specifically during untreated psychosis were associated with prolonged DUP. In line with Clarke et al. (2006) we found that the DUP became significantly longer with each level of increasingly severe suicidality, with a median DUP of more than four years for patients who attempted suicide during untreated psychosis.

Previous studies on the relationship between DUP and suicide attempts have yielded apparently inconsistent results. Some studies have found an association between longer DUP and suicide attempts (Altamura et al., 2003; Clarke et al., 2006; Harvey et al., 2008), while other studies have not (Bakst et al., 2009; Foley et al., 2008; Nordentoft et al., 2002). A recent study even found that shorter DUP was correlated with suicide attempts (Preti et al., 2009), but this finding could be explained by the exclusion of patients with substance dependency, a group with increased risk for suicide attempts (Verdoux et al., 1999) and prolonged DUP (Cougnard et al., 2004). Our finding of a relationship between prolonged DUP and higher risk for suicide attempts are in line with the only two studies that measured predictors of suicide attempts specifically during untreated psychosis (Clarke et al., 2006; Harvey et al., 2008). The studies that did not find a relationship between DUP and suicide attempts measured attempts in phases extending beyond the period of untreated psychosis, and our finding of a non-

relationship between DUP and attempted suicide prior to study entry is thus consistent with their findings. In sum, this finding from study II indicates that the duration of untreated psychosis has relevance for the suicide risk specifically during the period of untreated psychosis.

A possible explanation for the relationship between prolonged DUP and suicide attempts during untreated psychosis is that the DUP is a proxy factor for another variable associated with both the DUP and suicidal acts. For instance, Clarke et al. (2006) suggest that patients with long DUPs may have more malignant forms of illness likely to be associated with suicidality. If so, it is likely that DUP would be associated not only with suicide attempts during untreated psychosis, but also with suicide attempts prior to study entry. This was not the case in the present study. Other explanations for the association between DUP and suicide attempts during untreated psychosis could be longer opportunity time per se, or alternatively longer exposure to psychosis (Clarke et al., 2006). Experiencing psychotic symptoms is traumatic and distressing (Birchwood, 2003), and a majority of patients develop depression concurrent with acute psychosis (Birchwood, Iqbal, Chadwick, & Trower, 2000). Furthermore, a majority of patients experience loss of hope and aspirations, disruption, and social isolation as a consequence of onset of FEP (Tarrier, Khan, Cater, & Picken, 2007). In line with this, patients with FEP have diminished quality of life already at treatment start, and diminished quality of life has been associated with prolonged DUP (Browne et al., 2000). It is possible that experiencing psychotic- and related symptoms over longer periods of time, before treatment commences, increases the risk for attempting suicide. Finally, FEP-patients with poor premorbid functioning and at-risk behaviour (e.g. substance use) are more likely to have delayed treatment start and hence long DUP (Cougnard et al., 2004). It is possible that the patients with prolonged DUP in our study had levels of functioning or behaviours that delayed them from coming to treatment, unless they finally attempted suicide. Study II cannot conclude on this matter, as we did not register specifically whether suicidality was part of the reason for coming to treatment.

In sum, our findings indicate that the prevalence of suicidality in FEP-patients is high, especially during the period of untreated psychosis. Suicide attempts made during this period was associated with prolonged DUP.

5.1.3. Insight, beliefs about psychosis, and suicidality in first episode psychosis

Study III is the first to investigate the relationship between insight, beliefs about psychosis, depressive symptoms, and suicidality in a sample of FEP-patients. Nearly 46% of the patients were currently suicidal, in line with previous research showing that suicidality is common in patients with FEP (Nielssen & Large, 2009). We found that depressive symptoms did not mediate between insight and suicidality or between beliefs and suicidality, i.e. more current depressive symptoms, higher insight, and beliefs about negative outcomes for psychosis were independently related to current suicidality. Current depressive symptoms were strongly associated with current suicidality, in keeping with several other studies reporting that depression increases the risk for suicidal behaviour (Hawton et al., 2005a). Depression has been related to both insight and to negative beliefs in general, i.e. higher insight is associated with higher levels of depression (Mintz et al., 2003), and depression is characterised by negative cognitive biases, e.g. negative beliefs and attitudes (Beck, 2005). Thus, a possible explanation for the relationship between insight and suicidality could have been that patients with insight were more depressed and therefore more suicidal. Similarly, the relationship between negative beliefs about psychosis and suicidality could be explained by more negative beliefs reflecting more depression in the suicidal patients. However, this was not the case in study III; insight and beliefs about negative outcomes for psychosis were associated with current suicidality after controlling for the level of depressive symptoms. This indicates that although depression is clearly associated with suicidality, risk factors for suicidality in FEP-patients go beyond mere feelings of depression and include the patients' evaluations of their own personal disorder and of psychotic disorders in general.

Our finding of an association between higher insight and current suicidality is consistent with other studies (Foley et al., 2008; Robinson et al., 2009). Crumlish et al. (2005) found that insight at one point in time predicted later suicide attempts. Thus, a reasonable interpretation of our result is that higher overall insight may lead to suicidality. The finding that beliefs about negative outcomes for psychosis were associated with current suicidality is in keeping with a study finding a relationship between personal negative illness perceptions and suicidal ideation (Fialko et al., 2006). A plausible interpretation of our finding is that patients with FEP may view outcomes of psychotic disorders to be very negative, to the extent that suicide is considered a way out. We expected that only patients with high insight and negative beliefs

about psychosis would be suicidal, as negative beliefs about psychosis would have personal significance only to patients with high insight. Contrary to this expectation, we found that patients with higher insight had a higher risk of being suicidal regardless of their beliefs about psychosis. In view of this, it is noteworthy that some patients had not been informed about their diagnosis when they were assessed in the study. However, information about diagnosis does not automatically change level of insight, as indicated by the inconsistent effect of psychoeducation in achieving this goal (Henry & Ghaemi, 2004). Also, patients may be aware of having a mental disorder without knowing their exact diagnosis. Hence, it is unclear how variation in knowledge about diagnosis influenced the relationship between insight, beliefs about psychosis and suicidality in study III. An alternative and more probable explanation of our finding is that our measurement of beliefs did not tap self-stigmatising beliefs about psychosis, but rather more general beliefs about psychosis.

In sum, our findings indicate that more depressive symptoms, higher insight and negative beliefs about psychosis increase the risk for suicidality in FEP-patients.

5. 2. Discussion of general methodological issues

5.2.1. Sample issues; representativity and generalisability

We have studied samples of the population of patients with psychotic disorders, and biases in selecting our samples may have occurred. An important issue is to what degree the present samples are representative for the population of patients with psychotic disorders, and whether our findings can be generalised to this population.

The patients in the present studies were consecutively recruited from inpatient and outpatient psychiatric units. Mental health care in Norway is organised in catchment areas, and all inhabitants in a given catchment area are offered public mental health care. This system has the advantage of reducing the socio-demographical biases that may affect samples selected from either public or private treatment facilities, and increases the likelihood that our samples are representative for the population of patients with psychotic disorders. Furthermore, by recruiting patients from both in- and out patient units we were able to include patients in different phases of the disorder and with different levels of symptomatology, also increasing

the sample representativity. Patients were included as soon as possible, i.e. as soon as they were capable of completing the TOP assessment protocol. This excluded patients in the most acute phase of illness, for instance grossly disorganised or agitated patients. However, as the TOP inclusion period extends over several years and treatment units at different levels, the patients who were detected in very acute illness phases were offered participation at a later point in time. Of note is that the TOP study includes patients in treatment. Consequently, we have no data on patients with psychotic disorders who do not receive treatment, i.e. undetected cases or patients who receive treatment outside of psychiatric units, e.g. at general practitioners. However, as psychotic disorders are considered to be severe mental disorder, it can be assumed that most individuals with psychotic disorders will be connected with the psychiatric services at one point in time.

In recruiting patients to the TOP study, patients with a suspected or confirmed psychotic disorder were initially asked by their treating clinician if they were interested in study participation. The patients that were interested in participating were then referred to the TOP study assessment team. This ensured the rapid referral of a large group of patients. However, this procedure is dependent on the clinician's ability to recognize eligible patients and motivation to forward them to the assessment team. In order to facilitate the inclusion of all eligible patients, the members of the TOP assessment team were situated at the clinical units, and this made possible frequent contact between the clinical units and TOP study. Clinicians may have failed to recognize some patients as eligible, in particular patients with a first episode of psychosis with apparently unclear symptomatology. However, the close contact between clinicians and researchers made it possible to discuss potential cases, hence reducing the chance of missing eligible patients. Some clinicians may have refrained from referring patients to the study due to some form of scepticism. However, several patients passed the clinicians' pre-screening, but then turned out not to fulfil the inclusion criteria; e.g. they did not have a psychotic disorder. This phenomenon gave the impression that rather than referring too few patients, clinicians referred too many. Clinicians may have been motivated to refer patients by the thorough assessment the patients received, of which the results in most cases were reported to the clinicians. An overall impression was thus that eligible patients were referred to the TOP study, assuring the samples' representativity.

Some patients refused to participate in the TOP study; they refused when approached by their clinician or by TOP interviewers, and a very small group of patients declined to go further after an initial assessment. According to regulations from the Norwegian Data Inspectorate, we are not allowed to obtain information about patients who do not give informed consent, or who refuse to participate in a study. Hence, we have not registered the participation refusal rate and have no data on these patients. One alternative could have been to count the refusals anonymously. However, as some of the consenting patients who passed the clinicians' pre-screening turned out not to have psychotic disorder after all, we can assume that a share of the refusers also did not fulfil our inclusion criteria. Hence, counting the refusals without registering clinical data would potentially have given misleading information. One hypothesis is that the patients with most severe symptomatology and/or functioning are the ones who refused, leaving our sample to consist of the patients with lower symptom levels and better functioning. The inclusion of patients from in- and out patient units was carried out in order to ensure variation in symptomatology. It can be assumed that admitted patients have more severe symptoms than patients receiving outpatient treatment. Although this has not been investigated systematically, we have no indication that there were more refusers among patients receiving inpatient care than outpatient care, which may indicate that our sample is not biased regarding illness severity.

The representativity of the patients in the TOP study was investigated by comparing data with variables from the Ullevål 600 Health Care Study (Ringen et al., 2008). This survey included all patients from all psychiatric units at the former Ullevål University Hospital from May 2003 until May 2005 with psychotic and affective disorders (F 20 – F 39) according to the ICD-10 (WHO, 1993). The total sample included 1002 patients. The TOP sample was withdrawn, leaving 849 patients in the reference group. There were no differences in age or gender between the TOP sample and the reference group. Overall, this indicates that the TOP sample is representative for the population of patients with psychotic disorders .

Some studies include only patients at high risk for suicidality [e.g (Meltzer et al., 2003)], resulting in samples that are relatively homogenous regarding suicidal phenomena. However, to assure a representative sample, we did not select patients according to level of suicidality. The TOP sample thus consisted of patients who ranged from having no suicidality to having

severe suicidality, lifetime and currently, presumably reflecting the natural variance of suicidality in the study population. We also included patients with substance use in all three studies. This was done in order to assure a representative sample, as substance use is prevalent in patients with psychotic disorders (McCleery, Addington, & Addington, 2006). Studies on the effects of substance use on cognition in patients with psychotic disorders have yielded inconsistent results (Loberg & Hugdahl, 2009; Ringen et al., 2010); substance use has been associated with impaired neurocognitive function (Wobrock et al., 2007), but also with increased neurocognitive function (McCleery et al., 2006), and neither (Pencer & Addington, 2003). The association between prior substance use, neurocognitive function, and suicidality was analysed in study I, but we did not find substance use to be related to either suicidality or neurocognitive function. We have no reason to believe that the inclusion of substance users in the pursuit of a representative sample affected our results. In study I, we did exclude patients who did not have Norwegian as their first language, or who had not received all of their compulsory schooling in Norway. This was done in order to assure valid neuropsychological test performance. This meant excluding part of the migrant population, in which the rate of schizophrenia is known to be high (McGrath et al., 2004). It is unclear how these excluded patients may have differed from the included patients on issues of suicidality.

The samples in study II and III consisted of patients with a FEP. Patients in these samples were included up to 52 weeks following start of adequate treatment. The long inclusion period was established in order to recruit patients with different illness course, including patients with the most severe illness who needed time before they were able to participate in the study. The time since treatment start could thus potentially have differed considerably among the patients, and differing levels of suicidality could be a reflection of different duration of treatment. However, in study III we found that there was no significant difference between suicidal and non-suicidal patients in time since treatment start. Median time since treatment start for the whole sample was one month, while 75% were included no longer than 3 months after treatment start, indicating that the majority of patients was similar in being included in the study relatively close to treatment start. This was not explored specifically in study II, but we have no reason to believe that the two samples differ on this variable.

The samples in study II and III constituted of patients with a first episode of any functional psychotic disorder, including affective disorders with mood-incongruent psychotic symptoms. A possible consequence of this inclusion criterion is that the samples became too heterogeneous, masking important relationships between suicidality and subgroups. The inclusion of a range of psychotic disorders is in keeping with several other studies of FEP-patients (Clarke et al., 2006; Melle et al., 2006; Nordentoft et al., 2002). This made possible the recruitment within a limited time frame of a large number of patients from a group which basically has a relatively low incidence rate (McGrath et al., 2004), increasing the statistical power. However, the reason for this inclusion criterion goes beyond the goal of recruiting large samples. The group of patients with FEP vary considerably on a range of variables, e.g. age, symptoms, duration of symptoms, and affective symptoms. In samples like the present, where many patients have not yet remitted from their first episode of psychosis, diagnoses are potentially unstable. Studies report of a significant degree of diagnostic instability in FEP-patients (Baldwin et al., 2005; Haahr et al., 2008); i.e. as the illness proceeds, the diagnoses change. The inclusion of a broad range of diagnoses increases the likelihood of including all cases of psychotic disorders, and hence increases the representativity of the samples. In support of our strategy, the dichotomising of schizophrenia and bipolar disorder has been criticised due to overlapping symptomatology between psychotic and affective disorders (Craddock & Owen, 2007). Recent studies also indicate that schizophrenia and bipolar disorder may have common aetiology (Craddock et al., 2009). Finally, patients with schizophrenia and other psychotic disorders (Radomsky et al., 1999), and patients with bipolar disorders (Hawton et al., 2005b) are associated with elevated suicide rates. Based on this, it seemed reasonable to include patients with a range of psychotic disorders.

A measure that reduced the heterogeneity of the sample was to include only patients with affective disorders with mood-incongruent psychotic symptoms. Due to diagnostic instability, patients with affective psychosis (i.e. bipolar disorders or major depressive disorder) could at a later point in time be re-evaluated to have a schizoaffective disorder. This particularly applies to patients meeting the A-criterion for schizophrenia in DSM-IV (American Psychiatric Association, 1994), including bizarre psychotic symptoms and other mood-incongruent symptoms. According to the DSM-IV B-criterion for schizoaffective disorder, if these symptoms last more than two weeks in the absence of prominent mood symptoms, the

diagnosis may change to schizoaffective disorders. Because of this, patients with affective psychoses with mood-incongruent psychotic symptoms were included in the studies. A consequence of this is that our results cannot without further consideration be generalised to patients with affective disorders without psychotic symptoms or with mood-congruent psychotic symptoms.

5.2.2. Design issues; cause and effect

The design in the present studies was cross-sectional, with somewhat different consequences for interpretation of the results in the three studies. Overall, a cross-sectional design means lack of knowledge about the sequence of phenomena, thus limiting conclusions about cause and effect. In study I we assessed neurocognitive function when patients entered the study, and not concurrent with the suicide attempts. Neurocognitive impairments in schizophrenia are considered to be relatively stable over time (Heaton et al., 2001), but some studies suggest that neurocognitive function may be related to current suicidal state (LeGris & van Reekum, 2006; Marzuk et al., 2005; Westheide et al., 2008). Hence, the measurement of neurocognitive function may have been different if measured closer in time to the suicide attempts. Similarly, we cannot conclude on the causal relationship of our finding of an association between current suicidality and impulsivity (inhibitory control), mediated by positive symptoms. Within this design, we have no way of knowing whether the patients who were currently suicidal would be more impulsive also without suicidal symptoms. In order to conclude on this, we would have to measure impulsivity over time and across different states. Another limitation due to the cross-sectional design is that patients classified as non-attempters could be future suicide attempters. A potential number of future attempters now classified as non-attempters could thus possibly explain our finding of a non-difference between attempters and non-attempters. By following the patients over time, we would have had the opportunity to register future suicide attempts.

In study I, we measured lifetime occurrence of suicide attempts, and in study II, we measured suicidal ideation and attempts in different periods up until study entry. Suicidality was thus measured retrospectively, and information on past suicidality may have been affected by memory bias. It is likely that this would have affected data in study II the most, because patients were asked in more detail about different suicidal phenomena in different time

intervals. However, in both study I and II, the main analyses were conducted on suicide attempts, and information about suicide attempts were cross-checked in several sources, i.e. both from patients responding on specific questions about prevalence of suicidality over time (study II), responses to questions in the SCID-I interview (First et al., 1995), and hospital records (study I and II).

In study III we found an association between insight and suicidality, and between beliefs about psychosis and suicidality, but our cross-sectional design limits concluding on the causal direction of these relationships. This may have been possible if the phenomena had been studied over time. We cannot know whether increased insight led to suicidality, or whether suicidality led to higher insight. However, the latter scenario seems highly improbable; it is unlikely that suicidality pr se would increase insight into a psychotic disorder. Hence, we made the causative assumption that insight leads to suicidality in psychotic disorders. This assumption is also supported by a follow-up study finding that insight at one point in time predicted suicide attempts at follow-up (Crumlish et al., 2005). The same causal caveat applies to our finding of the relationship between beliefs about psychosis and suicidality; we cannot conclude whether negative beliefs led to suicidality or the opposite. It is possible that being suicidal involves having negative beliefs about future outcomes in general. However, this needs to be resolved within a research design that allows for studying the relationship between beliefs about psychosis and level of suicidality over time.

5.2.3. Measurement issues; validity and reliability

5.2.3.1. General clinical assessment

The main instruments used in the present studies are all widely accepted within psychosis research and have shown satisfactory psychometric properties (see Methods). In order to ensure reliable clinical assessments, all interviewers in the TOP study underwent a general training program for the main clinical instruments, i.e. SCID-I, PANSS and GAF. In addition, all interviewers received individual supervision on diagnostics from a specialist in psychology or psychiatry and diagnoses were also discussed at regular consensus meetings. As described in Methods, analyses of inter-rater reliability for the main instruments were conducted, and reliability was found to be satisfactory.

5.2.3.2. Neuropsychological assessment

The neurocognitive measures used in study I are also widely accepted and standardised tests, measuring domains known to be impaired in patients with psychotic disorders (Bilder et al., 2000). In addition to basic training in neuropsychological assessment, reliability was ensured by initial calibration of scoring, and supervision by a specialist in neuropsychology. A forced recognition task (CVLT-II) (Delis et al., 2004) was used in order to exclude patients with lack of test motivation. Overall, these means should ensure the validity and reliability of our assessments.

Reviews of literature have shown that neurocognitive functioning is related to several forms of functional outcome, e.g. occupational functioning, social attainment, and degree of independent living (Green et al., 2000; Green et al., 2004). Despite this, cognitive performance in a test-situation may be very different from cognitive functioning in a real-life setting, and this raises the question about the ecological validity of the neuropsychological assessments, i.e. to what degree is data obtained by our tests actually relevant for suicidal behaviour in the "real world"? Although the tests applied in this study are used extensively and considered to have sound psychometric properties, the validity of a test will vary with the use to which it is put (Lezak, 1995). Hence, whether our neuropsychological measures actually have bearing on suicidal behaviour outside of a test situation remains unclear. Furthermore, the neurocognitive test battery used in this study included measures of a range of neurocognitive domains shown to be impaired in psychotic disorders (Bilder et al., 2000). However, it is possible that other areas of neurocognitive function have more relevance for engaging in suicidal behaviour.

5.2.3.3. Assessment of suicidality

We measured different expressions of non-fatal suicidality in the present studies. Our main concern in focusing on suicidality in psychotic disorders is to increase knowledge in order to predict and prevent completed suicide. In view of this, it may be considered a derailment to study non-fatal suicidal behaviour. However, as noted in the Introduction, the study of completed suicide is methodologically challenging. Despite the elevated suicide risk, the number of patients with psychotic disorders who die by suicide is relatively low. The study of completed suicide thus involves recruiting very large samples, which in practice is difficult for several reasons, if not impossible (Meltzer et al., 2003). Moreover, post-mortem

investigations are potentially incomplete and always indirect, including data from other sources than the patients themselves. For these reasons, non-fatal suicidal behaviour is commonly studied in order to learn more about completed suicide. In support of this approach, research indicates that suicidal ideation, suicide attempts and completed suicide are associated with each other (Harkavy-Friedman et al., 1999; Hawton et al., 2005a; Nordentoft et al., 2002), and that suicidal behaviour of milder severity may be important phases in a process leading to completed suicide (Kontaxakis et al., 2004). In keeping with this, attempted suicide is found to be one of the most important predictors of completed suicide (Hawton et al., 2005a). However, McGirr and Turecki (2008) has pointed out that the rate of suicide attempts is greater than the rate of completes suicides, and consequently the predictors of attempted suicide may be dubious predictors of completed suicide. Studies have also indicated differences, i.e. patients who completed suicide differ from suicide attempters in being male (Harkavy-Friedman & Nelson, 1997), more depressed, hopeless, and socially isolated (Drake et al., 1986). Thus, whether we can apply our findings to completers of suicide remains to be clarified.

We chose to focus on suicide attempts rather than alternative concepts like DSH or parasuicide. Unlike DSH and parasuicide, a suicide attempt is defined by the presence of an intention to die. Acts classified as DSH and parasuicide will consequently include self-injurious behaviour that is more heterogeneous than behaviour classified as attempted suicide (Silverman, 2006), possibly comprising behaviour clearly without suicidal intent. However, the concept of intent is not easily measured; people can experience great ambivalence in their wish to die, and suicidal intent may fluctuate over time. Furthermore, accounts of suicidal intent after an attempt can be influenced by the context and the consequences of acknowledging the intent (McKeon, 2009). This could possibly lead to underreporting of suicidal attempts. Information on suicide attempts in the present studies was obtained from the patients' accounts and from hospital records. We may have missed information on suicide attempts not reported, but given that we got information from several sources, these are likely to be few.

We did not specifically measure the inter-rater reliability of the different suicidality measurements in the three studies. The likelihood that our data on attempted suicide are

reliable is increased by the fact mentioned above; patients' accounts were supplied with information from hospital records. Suicidal ideation, on the other hand, could not be double-checked in the same way, and may be more elusive and thus more difficult to assess. However, the IDS-C and CDSS used to assess current suicidality have overall been shown to have satisfactory psychometric properties in assessing depression (Addington et al., 1990; Addington, Addington, & Maticka-Tyndale, 1994; Addington, Addington, Maticka-Tyndale, & Joyce, 1992; Rush et al., 1996), which includes the assessment of level of current suicidality. Furthermore, we did measure inter-rater reliability for other instruments that include assessments of current suicidality, i.e. SCID-I, PANSS, and GAF. As the inter-rater reliability for these measurements were satisfactory, we can assume that suicidality assessments were also acceptable. Finally, the TOP protocol includes several questionnaires and interviews assessing current suicidality. It is likely that going over these questions several times enhanced the quality of the data.

Although the IDS-C and CDSS have shown overall satisfactory psychometric properties in measuring depression, the single suicidality items have not been validated per se. Suicidality rating scales are ultimately developed with the purpose of assessing suicide risk (Preston & Hansen, 2005). Although this is the overall aim in this field of research, our particular objective in the present studies was to assess the straightforward presence of suicidal ideation and acts the last 1 – 2 weeks; an objective that requires less information than the prediction of completed suicide. A related issue is the obvious general limitation in the study of suicidal ideation; the fact that it is only possible to assess the suicidal ideation that is actually disclosed. We have no way of knowing whether the patients held back information on current suicidal symptoms. It is possible that the assurance of confidential data handling, the thorough examination of different kinds of symptoms, and also touching upon the subject of suicidality several times during the clinical interview may have encouraged openness about suicidal phenomena.

In order to examine predictors of current suicidality in study III, a series of regression analyses was conducted. The dependent variable in these analyses was currently non-suicidal/suicidal, derived from the suicidality item on the CDSS. The currently non-suicidal and suicidal patients differed significantly on depressive symptoms, which were further

explored as independent variable in the regression analyses. In order to avoid suicidality as part of both independent and dependent variable, depression was measured as the CDSS total score minus the suicidality item, resulting in a measurement of depressive symptoms rather than depression. This was considered appropriate on the grounds that a diagnoses of DSM-IV major depressive episode (American Psychiatric Association, 1994) does not require the presence of suicidality, although suicidality is one of the possible symptoms. This underlines that depression and suicidality are related but not inseparable phenomena (Maris, 2002; Williams et al., 2005).

5.2.3.4. Measuring beliefs about psychosis

In study III we used the schizophrenia version of the Attitudes and Beliefs abut Mental Health problems (Jorm et al., 1999) to measure patients beliefs about psychosis. We translated this self-report questionnaire into Norwegian for the purpose of this study, and translated it back into English to ensure proper translation, with the approval of the author. The questions in this questionnaire were all based on a vignette describing a young man with symptoms fulfilling ICD-10 (WHO, 1993) and DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia. It could be argued that patients with lack of insight into their own psychotic symptoms may also have difficulty recognising psychotic illness in others. However, the level of insight in our sample varied, with the median PANSS insight score of 3, indicating partial insight. Furthermore, almost 67% of the sample recognised and labelled the described symptoms as psychotic, and an additional 18% recognised some kind of mental disorder, but without being able to classify it as psychosis. Of note is also previous findings indicating that the recognition of others' psychotic symptoms is independent of insight into own illness (Startup, 1997). Taken together, this indicates that patients with psychotic disorders are capable of recognizing psychotic illness in others.

5.3. Strengths, limitations, and future research

The strength of this thesis is that the present studies included relatively large catchment area-based samples of patients with psychotic disorders, consecutively recruited from both in- and outpatient psychiatric units, and with heterogeneity in both suicidal and other clinical symptoms. This increases the likelihood that the samples were representative of the

population of patients with psychotic disorders. Furthermore, all patients underwent comprehensive clinical and neuropsychological assessments, resulting in thoroughly described samples, and the reliability of our main measurements were found to be good. An additional strength was that we measured both lifetime suicide attempts and current suicidality in study I, and were thus able to control for the possible confounding effect of current suicidal state on the relationship between neurocognition and suicide attempts.

The overall aim of this thesis was to identify possible risk factors for suicidal behaviour, which is important in order to prevent self-inflicted deaths in patients with psychotic disorders. The main limitation of the thesis is thus that we did not focus on completed suicide, but rather on proxy measures of suicide, i.e. suicidal ideation and suicide attempts. On the one side, studies have shown that both suicidal ideation and attempts are associated with completed suicide (Hawton et al., 2005), indicating that our findings may have relevance not only for suicidal ideation and attempts, but also for suicide. On the other hand, studies have indicated that suicide attempters differ from completers in some respects (Drake et al., 1986; Harkavy-Friedman & Nelson, 1997). Applying our results to completed suicide should thus be done with caution.

A possible limitation if more specific nature is that we did not have the same measurement of current suicidality for all the patients in study I, and therefore had to use suicidality scores from the IDS-S (Rush et al., 1996) and the CDSS (Addington et al., 1990). For the 26 patients who were evaluated with both questionnaires, suicidality scores were incongruent for four patients. This incongruence could have been an indication of poor inter rater-reliability in assessing current suicidality. However, the IDS-C measure symptoms the last week, while CDSS measure symptoms the last two weeks, and this discrepancy probably accounts for the incongruent suicidality scores. Another possible limitation is that we used retrospectively measured suicidality in some analyses, and data on timing of suicidal behaviour could have been affected by memory bias. However, the main analyses involved suicide attempts, and information on suicide attempts were cross-checked in multiple sources. The cross-sectional design of our studies limits inferences about the causal direction of relationships, e.g. between insight and suicidality and between beliefs about psychosis and suicidality. Interpretation of

our findings is also partly limited by the use of PANSS in assessing insight, as it measures overall insight rather than different dimensions of insight (Wiffen et al., 2010).

The finding of an association between current suicidal state and impulsivity mediated by positive symptoms clearly indicates that in line with our study, future studies should include measures of current suicidality when investigating the relationship between neurocognition and suicidality. To further explore this finding, prospective studies are warranted in order to follow the concurrent development of suicidality, clinical symptoms and neurocognitive performance. One possible explanation for not finding a relationship between impulsivity and suicide attempts is that impulsivity could be less stable than originally thought (Gut-Fayand et al., 2001). This implies that future research on the relationship between impulsivity and suicidal behaviour should make use of both trait and state measures of impulsivity. Furthermore, future research on cognition in suicidal patients with schizophrenia should in addition focus on aspects more directly linked to suicidal processes.

Our findings suggest that IQ, executive functioning, and impulsivity as separate cognitive domains are not related to suicidal behaviour. However, suicidal behaviour has been related to biases in reasoning, for instance a tendency to "jump to conclusions", in which impulsivity may play a part. Also, suicidal individuals are shown to have poor abilities in interpersonal problem solving, which may be related to impairments in executive functioning (Bolton et al., 2007). Hence, future research on cognition and suicidality may benefit from investigating the interaction between different cognitive domains and their relationship to suicidal behaviour.

Some studies report that only aspects of insight are associated with suicidal behaviour (Amador et al., 1996; Crumlish et al., 2005; Schwartz & Smith, 2004). A suggestion for future research is to use a multidimensional insight scale, e.g. measuring recognition of having a mental illness, the need for treatment, and ability to recognise symptoms as separate domains. This may provide more specific information on the mechanism of the relationship between insight and suicidality. Our unexpected finding that higher insight increases the risk for suicidality regardless of beliefs about psychosis could be explained by our study possibly measuring more general beliefs about psychosis, and not self-stigmatising beliefs about

psychosis. In order to investigate this further, future research should include methods that specifically measure beliefs about the patients' own illness.

5.4. Implications

The findings of this thesis may have implications for interventions to prevent suicidality. The lack of relationship between neurocognitive function and suicide attempts implies that assessment of suicide risk should be conducted irrespective of whether patients present evidence of cognitive impairment or not. The association between prolonged DUP and increased risk for attempting suicide during untreated psychosis is of importance as it indicates that early intervention, with the intent to reduce DUP, could have a specific effect on preventing suicidal behaviour. Furthermore, we found a relationship between suicide attempts and depressive episodes and between current depressive symptoms and current suicidality. These findings underline the need to assess and treat depression in FEP-patients. However, our findings also suggest that merely treating depression is not sufficient in order to prevent suicidality. The association between higher insight and suicidality indicates that insight should be monitored as part of assessing the risk for suicidal behaviour. It also implies that treatment should persist during phases when insight is gained, even if increase in level of insight coincides with the waning of psychotic symptoms. Finally, the finding of an association between negative beliefs about psychosis and suicidality suggest a need to counteract negative beliefs about psychosis. Although psychotic disorders have a severe course for some patients, research shows that a significant proportion of patients treated for schizophrenia achieve favourable long term outcome (Harrison et al., 2001). Interventions aimed at modifying negative beliefs about psychoses may have the effect of reducing the risk for suicidality in patients with psychotic disorders.

6. CONCLUSION

The studies in this theses investigated possible demographical, clinical, and neuropsychological risk factors for suicidal behavior in patients with psychotic disorders, with special emphasis on patients with a first episode of psychosis.

Suicide attempts in patients with schizophrenia spectrum disorders were not associated with IQ, executive function, neuropsychologically measured impulsivity, or any other neurocognitive domain. This suggests that neurocognition does not play an essential part of a predisposition to attempt suicide, at least not the domains measured in this study.

In contrast, several clinical variables were related to suicidality, and the variables differed somewhat for different time intervals. The findings confirmed a high prevalence of suicidality in patients with a first episode of psychosis, and the occurrence of suicidality was particularly high during the period of untreated psychosis. Attempted suicide prior to study entry was associated with female gender, younger age at psychosis onset, more depressive episodes, and a history of alcohol disorder. Attempting suicide during the period of untreated psychosis was also associated with more depressive episodes and younger age at psychosis onset, and in addition the use of drugs the last six months prior to study entry. The most important difference between suicide attempts prior to study entry and during the period of untreated psychosis was that only suicide attempts made specifically during untreated psychosis were associated with prolonged DUP.

Depressive symptoms did not mediate between insight and suicidality, or between beliefs about psychosis and suicidality in FEP-patients, i.e., more depressive symptoms, higher insight, and negative beliefs about psychosis were independently associated with current suicidality. Lastly, beliefs about psychosis did not moderate the relationship between insight and suicidality; thus, FEP-patients with higher insight were at higher risk for being suicidal, regardless of their beliefs about psychosis.

In conclusion, the particularly high prevalence of suicidality during the period of untreated psychosis, and the significance of a prolonged DUP for suicide attempts, indicate that timing is an essential feature of interventions to prevent suicidal behavior, specifically suggesting a

need to focus on the period of untreated psychosis. Furthermore, suicidality in psychotic disorders seems to be determined by multiple factors. Some factors, like depression and substance use, are risk factors for suicidality that patients with psychotic disorders have in common with the general population. Other factors, like prolonged DUP, illness insight and beliefs about psychosis, are more specifically related to psychotic illness. This suggests that interventions aimed at preventing suicidal behavior in patients with psychotic disorders must be multifaceted and include strategies that specifically target patients with psychotic disorders.

7. REFERENCES

Addington, D., Addington, J., & Maticka-Tyndale, E. (1994). Specificity of the Calgary Depression Scale for schizophrenics. *Schizophrenia Research, 11,* 239-244.

Addington, D., Addington, J., Maticka-Tyndale, E., & Joyce, J. (1992). Reliability and validity of a depression rating scale for schizophrenics. *Schizophrenia Research, 6,* 201-208.

Addington, D., Addington, J., & Schissel, B. (1990). A depression rating scale for schizophrenics. *Schizophrenia Research, 3,* 247-251.

Addington, J., Williams, J., Young, J., & Addington, D. (2004). Suicidal behaviour in early psychosis. *Acta Psychiatrica Scandinavica, 109,* 116-120.

Altamura, A. C., Bassetti, R., Bignotti, S., Pioli, R., & Mundo, E. (2003). Clinical variables related to suicide attempts in schizophrenic patients: a retrospective study. *Schizophrenia Research, 60,* 47-55.

Amador, X. F., Flaum, M., Andreasen, N. C., Strauss, D. H., Yale, S. A., Clark, S. C. et al. (1994). Awareness of illness in schizophrenia and schizoaffective and mood disorders. *Archives of General Psychiatry, 51,* 826-836.

Amador, X. F., Friedman, J. H., Kasapis, C., Yale, S. A., Flaum, M., & Gorman, J. M. (1996). Suicidal behavior in schizophrenia and its relationship to awareness of illness. *American Journal of Psychiatry, 153,* 1185-1188.

Amador, X. F. & Gorman, J. M. (1998). Psychopathologic domains and insight in schizophrenia. *Psychiatric Clinics of North America, 21,* 27-42.

American Psychiatric Association (1994). *Diagnostic and statistical Manual of Mental Disorders, Fourth Edition*. Washington, D.C: American Psychiatric Association.

American Psychiatric Association (2003). Practice guideline for the assessment and treatment of patients with suicidal behaviors. *American Journal of Psychiatry, 160,* 1-60.

Angermeyer, M. C. & Dietrich, S. (2006). Public beliefs about and attitudes towards people with mental illness: a review of population studies. *Acta Psychiatrica Scandinavica, 113,* 163-179.

Baca-Garcia, E., az-Sastre, C., Garcia, R. E., Blasco, H., Braquehais, C. D., Oquendo, M. A. et al. (2005). Suicide attempts and impulsivity. *European Archives of Psychiatry and Clinical Neuroscience, 255,* 152-156.

Bakst, S., Rabinowitz, J., & Bromet, E. J. (2009). Antecedents and Patterns of Suicide Behavior in First-Admission Psychosis. *Schizophrenia Bulletin*.

Baldwin, P., Browne, D., Scully, P. J., Quinn, J. F., Morgan, M. G., Kinsella, A. et al. (2005). Epidemiology of first-episode psychosis: illustrating the challenges across diagnostic

boundaries through the Cavan-Monaghan study at 8 years. *Schizophrenia Bulletin, 31,* 624-638.

Beautrais, A. L. (2004). Further suicidal behavior among medically serious suicide attempters. *Suicide and Life-Threatening Behavior, 34,* 1-11.

Beck, A. T. (2005). The current state of cognitive therapy: a 40-year retrospective. *Archives of General Psychiatry, 62,* 953-959.

Bertelsen, M., Jeppesen, P., Petersen, L., Thorup, A., Ohlenschlaeger, J., le, Q. P. et al. (2007). Suicidal behaviour and mortality in first-episode psychosis: the OPUS trial. *British Journal of Psychiatry.Supplement, 51,* s140-s146.

Bertolote, J. M., Fleischmann, A., De, L. D., & Wasserman, D. (2004). Psychiatric diagnoses and suicide: revisiting the evidence. *Crisis, 25,* 147-155.

Bilder, R. M., Goldman, R. S., Robinson, D., Reiter, G., Bell, L., Bates, J. A. et al. (2000). Neuropsychology of first-episode schizophrenia: initial characterization and clinical correlates. *American Journal of Psychiatry, 157,* 549-559.

Birchwood, M. (2003). Pathways to emotional dysfunction in first-episode psychosis. *British Journal of Psychiatry, 182,* 373-375.

Birchwood, M., Iqbal, Z., Chadwick, P., & Trower, P. (2000). Cognitive approach to depression and suicidal thinking in psychosis. 1. Ontogeny of post-psychotic depression. *British Journal of Psychiatry, 177,* 516-521.

Bleuler, E. (1911). *Dementia Praecox oder die Gruppe der Schizophrenien*. Leipzig: Deuticke.

Bolton, C., Gooding, P., Kapur, N., Barrowclough, C., & Tarrier, N. (2007). Developing psychological perspectives of suicidal behaviour and risk in people with a diagnosis of schizophrenia: we know they kill themselves but do we understand why? *Clinical Psychology Review, 27,* 511-536.

Borges, G., Angst, J., Nock, M. K., Ruscio, A. M., Walters, E. E., & Kessler, R. C. (2006). A risk index for 12-month suicide attempts in the National Comorbidity Survey Replication (NCS-R). *Psychological Medicine, 36,* 1747-1757.

Bostwick, J. M. & Pankratz, V. S. (2000). Affective disorders and suicide risk: a reexamination. *American Journal of Psychiatry, 157,* 1925-1932.

Bourgeois, M., Swendsen, J., Young, F., Amador, X., Pini, S., Cassano, G. B. et al. (2004). Awareness of disorder and suicide risk in the treatment of schizophrenia: results of the international suicide prevention trial. *American Journal of Psychiatry, 161,* 1494-1496.

Brezo, J., Paris, J., & Turecki, G. (2006). Personality traits as correlates of suicidal ideation, suicide attempts, and suicide completions: a systematic review. *Acta Psychiatrica Scandinavica, 113,* 180-206.

Brown, S. (1997). Excess mortality of schizophrenia. A meta-analysis. *British Journal of Psychiatry, 171,* 502-508.

Browne, S., Clarke, M., Gervin, M., Waddington, J. L., Larkin, C., & O'Callaghan, E. (2000). Determinants of quality of life at first presentation with schizophrenia. *British Journal of Psychiatry, 176,* 173-176.

Bryan, C. J. (2007). Re: Neuropsychology of BPI and BPII. *Journal of Affective Disorders, 103,* 283, author-4.

Buckley, P. F., Miller, B. J., Lehrer, D. S., & Castle, D. J. (2009). Psychiatric comorbidities and schizophrenia. *Schizophrenia Bulletin, 35,* 383-402.

Burvill, P. W. (1998). Migrant suicide rates in Australia and in country of birth. *Psychological Medicine, 28,* 201-208.

Caldwell, C. B. & Gottesman, I. I. (1990). Schizophrenics kill themselves too: a review of risk factors for suicide. *Schizophrenia Bulletin, 16,* 571-589.

Cannon-Spoor, H. E., Potkin, S. G., & Wyatt, R. J. (1982). Measurement of premorbid adjustment in chronic schizophrenia. *Schizophrenia Bulletin, 8,* 470-484.

Carroll, A., Pantelis, C., & Harvey, C. (2004). Insight and hopelessness in forensic patients with schizophrenia. *Australian and New Zealand Journal of Psychiatry, 38,* 169-173.

Cavanagh, J. T., Carson, A. J., Sharpe, M., & Lawrie, S. M. (2003). Psychological autopsy studies of suicide: a systematic review. *Psychological Medicine, 33,* 395-405.

Cherpitel, C. J., Borges, G. L., & Wilcox, H. C. (2004). Acute alcohol use and suicidal behavior: a review of the literature. *Alcoholism, Clinical and Experimental Research, 28,* 18S-28S.

Cheung, A. M., Mitsis, E. M., & Halperin, J. M. (2004). The relationship of behavioral inhibition to executive functions in young adults. *Journal of Clinical and Experimental Neuropsychology, 26,* 393-404.

Clarke, M., Whitty, P., Browne, S., Mc, T. O., Kinsella, A., Waddington, J. L. et al. (2006). Suicidality in first episode psychosis. *Schizophrenia Research, 86,* 221-225.

Clement, S. & Foster, N. (2008). Newspaper reporting on schizophrenia: a content analysis of five national newspapers at two time points. *Schizophrenia Research, 98,* 178-183.

Conner, K. R. & Duberstein, P. R. (2004). Predisposing and precipitating factors for suicide among alcoholics: empirical review and conceptual integration. *Alcoholism, Clinical and Experimental Research, 28,* 6S-17S.

Coryell, W. & Young, E. A. (2005). Clinical predictors of suicide in primary major depressive disorder. *Journal of Clinical Psychiatry, 66,* 412-417.

Cougnard, A., Kalmi, E., Desage, A., Misdrahi, D., Abalan, F., Brun-Rousseau, H. et al. (2004). Pathways to care of first-admitted subjects with psychosis in South-Western France. *Psychological Medicine, 34,* 267-276.

Craddock, N., O'Donovan, M. C., & Owen, M. J. (2009). Psychosis genetics: modeling the relationship between schizophrenia, bipolar disorder, and mixed (or "schizoaffective") psychoses. *Schizophrenia Bulletin, 35,* 482-490.

Craddock, N. & Owen, M. J. (2007). Rethinking psychosis: the disadvantages of a dichotomous classification now outweigh the advantages. *World Psychiatry, 6,* 84-91.

Crisp, A. H., Gelder, M. G., Rix, S., Meltzer, H. I., & Rowlands, O. J. (2000). Stigmatisation of people with mental illnesses. *British Journal of Psychiatry, 177,* 4-7.

Crow, T. J. (1986). The continuum of psychosis and its implication for the structure of the gene. *British Journal of Psychiatry, 149,* 419-429.

Crumlish, N., Whitty, P., Kamali, M., Clarke, M., Browne, S., McTigue, O. et al. (2005). Early insight predicts depression and attempted suicide after 4 years in first-episode schizophrenia and schizophreniform disorder. *Acta Psychiatrica Scandinavica, 112,* 449-455.

Cuesta, M. J., Peralta, V., & Zarzuela, A. (2000). Reappraising insight in psychosis. Multi-scale longitudinal study. *British Journal of Psychiatry, 177,* 233-240.

David, A. S. (1990). Insight and psychosis. *British Journal of Psychiatry, 156,* 798-808.

De Hert, M., McKenzie, K., & Peuskens, J. (2001). Risk factors for suicide in young people suffering from schizophrenia: a long-term follow-up study. *Schizophrenia Research, 47,* 127-134.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2005). *The Delis-Kaplan Executive Function System (D-KEFS), Norwegian Manual.* Stockholm: Pearson Assessment.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2004). *California Verbal Learning Test - Second edition (CVLT-II). Norwegian Manual supplement.* Stockholm: Pearson Assessment.

Denning, D. G., Conwell, Y., King, D., & Cox, C. (2000). Method choice, intent, and gender in completed suicide. *Suicide and Life-Threatening Behavior, 30,* 282-288.

Dougherty, D. M., Mathias, C. W., Marsh, D. M., Papageorgiou, T. D., Swann, A. C., & Moeller, F. G. (2004). Laboratory measured behavioral impulsivity relates to suicide attempt history. *Suicide and Life-Threatening Behavior, 34,* 374-385.

Drake, R. E., Gates, C., & Cotton, P. G. (1986). Suicide among schizophrenics: a comparison of attempters and completed suicides. *British Journal of Psychiatry, 149,* 784-787.

Duberstein, P. R. & Conwell, Y. (1997). Personality disorders and completed suicide: a methodological and conceptual review. *Clinical psychology: science and practice, 4,* 359-376.

Eack, S. M. & Newhill, C. E. (2007). Psychiatric symptoms and quality of life in schizophrenia: a meta-analysis. *Schizophrenia Bulletin, 33,* 1225-1237.

Enticott, P. G. & Ogloff, J. R. P. (2006). Elucidation of impulsivity. *Australian Psychologist, 41,* 3-14.

Enticott, P. G., Ogloff, J. R. P., & Bradshaw, J. L. (2006). Associations between laboratory measures of executive inhibitory control and self-reported impulsivity. *Personality and Individual Differences, 41,* 285-294.

Erlenmeyer-Kimling, L., Rock, D., Roberts, S. A., Janal, M., Kestenbaum, C., Cornblatt, B. et al. (2000). Attention, memory, and motor skills as childhood predictors of schizophrenia-related psychoses: the New York High-Risk Project. *American Journal of Psychiatry, 157,* 1416-1422.

Evans, J., Platts, H., & Liebenau, A. (1996). Impulsiveness and deliberate self-harm: a comparison of "first-timers' and "repeaters'. *Acta Psychiatrica Scandinavica, 93,* 378-380.

Falloon, I. R. (1992). Early intervention for first episodes of schizophrenia: a preliminary exploration. *Psychiatry, 55,* 4-15.

Fenton, W. S. (2000). Depression, suicide, and suicide prevention in schizophrenia. *Suicide and Life-Threatening Behavior, 30,* 34-49.

Fialko, L., Freeman, D., Bebbington, P. E., Kuipers, E., Garety, P. A., Dunn, G. et al. (2006). Understanding suicidal ideation in psychosis: findings from the Psychological Prevention of Relapse in Psychosis (PRP) trial. *Acta Psychiatrica Scandinavica, 114,* 177-186.

First, M., Spitzer, R., Gibbon, M., & Williams, J. B. W. (1995). *Structured Clinical Interview for DSM-IV Axis I Disorders: Patient Edition (SCID-P), Version 2*. New York, NY: New York State Psychiatric Institute, Biometrics Research.

Foley, S., Jackson, D., McWilliams, S., Renwick, L., Sutton, M., Turner, N. et al. (2008). Suicidality prior to presentation in first-episode psychosis. *Early Intervention in Psychiatry, 2,* 242-246.

Green, M. F., Kern, R. S., Braff, D. L., & Mintz, J. (2000). Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? *Schizophrenia Bulletin, 26,* 119-136.

Green, M. F., Kern, R. S., & Heaton, R. K. (2004). Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophrenia Research, 72,* 41-51.

Gut-Fayand, A., Dervaux, A., Olie, J. P., Loo, H., Poirier, M. F., & Krebs, M. O. (2001). Substance abuse and suicidality in schizophrenia: a common risk factor linked to impulsivity. *Psychiatry Research, 102,* 65-72.

Haahr, U., Friis, S., Larsen, T. K., Melle, I., Johannessen, J. O., Opjordsmoen, S. et al. (2008). First-episode psychosis: diagnostic stability over one and two years. *Psychopathology, 41,* 322-329.

Harkavy-Friedman, J. M., Kimhy, D., Nelson, E. A., Venarde, D. F., Malaspina, D., & Mann, J. J. (2003). Suicide attempts in schizophrenia: the role of command auditory hallucinations for suicide. *Journal of Clinical Psychiatry, 64,* 871-874.

Harkavy-Friedman, J. M. & Nelson, E. (1997). Management of the suicidal patient with schizophrenia. *Psychiatric Clinics of North America, 20,* 625-640.

Harkavy-Friedman, J. M., Restifo, K., Malaspina, D., Kaufmann, C. A., Amador, X. F., Yale, S. A. et al. (1999). Suicidal behavior in schizophrenia: characteristics of individuals who had and had not attempted suicide. *American Journal of Psychiatry, 156,* 1276-1278.

Harrison, G., Hopper, K., Craig, T., Laska, E., Siegel, C., Wanderling, J. et al. (2001). Recovery from psychotic illness: a 15- and 25-year international follow-up study. *British Journal of Psychiatry, 178,* 506-517.

Harvey, P. D., Parrella, M., White, L., Mohs, R. C., Davidson, M., & Davis, K. L. (1999). Convergence of cognitive and adaptive decline in late-life schizophrenia. *Schizophrenia Research, 35,* 77-84.

Harvey, S. B., Dean, K., Morgan, C., Walsh, E., Demjaha, A., Dazzan, P. et al. (2008). Self-harm in first-episode psychosis. *British Journal of Psychiatry, 192,* 178-184.

Hasson-Ohayon, I., Kravetz, S., Roe, D., David, A. S., & Weiser, M. (2006). Insight into psychosis and quality of life. *Comprehensive Psychiatry, 47,* 265-269.

Haw, C., Hawton, K., Sutton, L., Sinclair, J., & Deeks, J. (2005). Schizophrenia and deliberate self-harm: a systematic review of risk factors. *Suicide and Life-Threatening Behavior, 35,* 50-62.

Hawton, K., Appleby, L., Platt, S., Foster, T., Cooper, J., Malmberg, A. et al. (1998). The psychological autopsy approach to studying suicide: a review of methodological issues. *Journal of Affective Disorders, 50,* 269-276.

Hawton, K., Sutton, L., Haw, C., Sinclair, J., & Deeks, J. J. (2005a). Schizophrenia and suicide: systematic review of risk factors. *British Journal of Psychiatry, 187,* 9-20.

Hawton, K., Sutton, L., Haw, C., Sinclair, J., & Harriss, L. (2005b). Suicide and attempted suicide in bipolar disorder: a systematic review of risk factors. *Journal of Clinical Psychiatry, 66,* 693-704.

Hawton, K. & Van Heeringen, K. (2009). Suicide. *Lancet, 373,* 1372-1381.

Heaton, R. K., Gladsjo, J. A., Palmer, B. W., Kuck, J., Marcotte, T. D., & Jeste, D. V. (2001). Stability and course of neuropsychological deficits in schizophrenia. *Archives of General Psychiatry, 58,* 24-32.

Heila, H., Isometsa, E. T., Henriksson, M. M., Heikkinen, M. E., Marttunen, M. J., & Lonnqvist, J. K. (1997). Suicide and schizophrenia: a nationwide psychological autopsy study on age- and sex-specific clinical characteristics of 92 suicide victims with schizophrenia. *American Journal of Psychiatry, 154,* 1235-1242.

Helgason, L. (1990). Twenty years' follow-up of first psychiatric presentation for schizophrenia: what could have been prevented? *Acta Psychiatrica Scandinavica, 81,* 231-235.

Henry, C. & Ghaemi, S. N. (2004). Insight in psychosis: a systematic review of treatment interventions. *Psychopathology, 37,* 194-199.

Horesh, N. (2001). Self-report vs. computerized measures of impulsivity as a correlate of suicidal behavior. *Crisis, 22,* 27-31.

Iqbal, Z., Birchwood, M., Chadwick, P., & Trower, P. (2000). Cognitive approach to depression and suicidal thinking in psychosis. 2. Testing the validity of a social ranking model. *British Journal of Psychiatry, 177,* 522-528.

Ivleva, E., Thaker, G., & Tamminga, C. A. (2008). Comparing genes and phenomenology in the major psychoses: schizophrenia and bipolar 1 disorder. *Schizophrenia Bulletin, 34,* 734-742.

Jorm, A. F., Korten, A. E., Jacomb, P. A., Christensen, H., & Henderson, S. (1999). Attitudes towards people with a mental disorder: a survey of the Australian public and health professionals. *Australian and New Zealand Journal of Psychiatry, 33,* 77-83.

Karatzias, T., Gumley, A., Power, K., & O'Grady, M. (2007). Illness appraisals and self-esteem as correlates of anxiety and affective comorbid disorders in schizophrenia. *Comprehensive Psychiatry, 48,* 371-375.

Karch, D. L., Barker, L., & Strine, T. W. (2006). Race/ethnicity, substance abuse, and mental illness among suicide victims in 13 US states: 2004 data from the National Violent Death Reporting System. *Injury Prevention, 12 Suppl 2,* ii22-ii27.

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia Bulletin, 13,* 261-276.

Kay, S. R. (1991). *Positive and negative syndromes in schizophrenia: assessment and research*. New York: Brunner/Mazel.

Keefe, R. S., Bilder, R. M., Harvey, P. D., Davis, S. M., Palmer, B. W., Gold, J. M. et al. (2006). Baseline neurocognitive deficits in the CATIE schizophrenia trial. *Neuropsychopharmacology, 31,* 2033-2046.

Keefe, R. S., Eesley, C. E., & Poe, M. P. (2005). Defining a cognitive function decrement in schizophrenia. *Biological Psychiatry, 57,* 688-691.

Keefe, R. S. & Fenton, W. S. (2007). How should DSM-V criteria for schizophrenia include cognitive impairment? *Schizophrenia Bulletin, 33,* 912-920.

Kerkhof, J. F. M. (2000). Attempted Suicide: Patterns and Trends. In K.Hawton & K. Van Heeringen (Eds.), *The International Handbook of Suicide and Attempted Suicide* (pp. 49-64). Chichester: John Wiley & Sons, Ltd.

Kerns, J. G., Nuechterlein, K. H., Braver, T. S., & Barch, D. M. (2008). Executive functioning component mechanisms and schizophrenia. *Biological Psychiatry, 64,* 26-33.

Kessler, R. C., Borges, G., & Walters, E. E. (1999). Prevalence of and risk factors for lifetime suicide attempts in the National Comorbidity Survey. *Archives of General Psychiatry, 56,* 617-626.

Kim, C. H., Jayathilake, K., & Meltzer, H. Y. (2003). Hopelessness, neurocognitive function, and insight in schizophrenia: relationship to suicidal behavior. *Schizophrenia Research, 60,* 71-80.

Kirkbride, J. B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J. et al. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. *Archives of General Psychiatry, 63,* 250-258.

Kontaxakis, V., Havaki-Kontaxaki, B., Margariti, M., Stamouli, S., Kollias, C., & Christodoulou, G. (2004). Suicidal ideation in inpatients with acute schizophrenia. *Canadian Journal of Psychiatry.Revue Canadienne de Psychiatrie, 49,* 476-479.

Kraepelin, E. (1899). *Psychiatrie: ein Lehrbuch fnr Studirende und Aerzte*. (vols. 6. vollstendig umgearb. Aufl.) Leipzig: J.A.Barth.

Kraepelin, E. (1920). Patterns of Mental Disorder/Die Erscheinungsform des Irreseins'. Zschr Ges Neurol Psychiat. 62, 1-29. In S.Hirsch & M. Shepard (Eds.), *Themes and variations in European psychiatry, 1974* (pp. 7-30). Bristol: John Wright & Sons.

Kuo, W. H., Gallo, J. J., & Tien, A. Y. (2001). Incidence of suicide ideation and attempts in adults: the 13-year follow-up of a community sample in Baltimore, Maryland. *Psychological Medicine, 31,* 1181-1191.

Lacro, J. P., Dunn, L. B., Dolder, C. R., Leckband, S. G., & Jeste, D. V. (2002). Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *Journal of Clinical Psychiatry, 63,* 892-909.

Larsen, T. K., Melle, I., Auestad, B., Friis, S., Haahr, U., Johannessen, J. O. et al. (2006). Substance abuse in first-episode non-affective psychosis. *Schizophrenia Research, 88,* 55-62.

LeGris, J. & van Reekum, R. (2006). The neuropsychological correlates of borderline personality disorder and suicidal behaviour. *Canadian Journal of Psychiatry.Revue Canadienne de Psychiatrie, 51,* 131-142.

Leucht, S., Burkard, T., Henderson, J., Maj, M., & Sartorius, N. (2007). Physical illness and schizophrenia: a review of the literature. *Acta Psychiatrica Scandinavica, 116,* 317-333.

Levi, F., La, V. C., Lucchini, F., Negri, E., Saxena, S., Maulik, P. K. et al. (2003). Trends in mortality from suicide, 1965-99. *Acta Psychiatrica Scandinavica, 108,* 341-349.

Lezak, M. D. (1995). *Neuropsychological assessment*. (vols. 3rd ed.) New York: Oxford University Press.

Lichtenstein, P., Yip, B. H., Bjork, C., Pawitan, Y., Cannon, T. D., Sullivan, P. F. et al. (2009). Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. *Lancet, 373,* 234-239.

Linden, M. & Godemann, F. (2007). The differentiation between 'lack of insight' and 'dysfunctional health beliefs' in schizophrenia. *Psychopathology, 40,* 236-241.

Loberg, E. M. & Hugdahl, K. (2009). Cannabis use and cognition in schizophrenia. *Frontiers in Human Neuroscience, 3,* 53.

Loebel, A. D., Lieberman, J. A., Alvir, J. M., Mayerhoff, D. I., Geisler, S. H., & Szymanski, S. R. (1992). Duration of psychosis and outcome in first-episode schizophrenia. *American Journal of Psychiatry, 149,* 1183-1188.

Lysaker, P. H., Bryson, G. J., & Bell, M. D. (2002). Insight and work performance in schizophrenia. *Journal of Nervous and Mental Disease, 190,* 142-146.

Lysaker, P. H., Roe, D., & Yanos, P. T. (2007). Toward understanding the insight paradox: internalized stigma moderates the association between insight and social functioning, hope, and self-esteem among people with schizophrenia spectrum disorders. *Schizophrenia Bulletin, 33,* 192-199.

Malenfant, E. C. (2004). Suicide in Canada's immigrant population. *Health Reports, 15,* 9-17.

Mann, J. J. (2002). A current perspective of suicide and attempted suicide. *Annals of Internal Medicine, 136,* 302-311.

Mann, J. J., Apter, A., Bertolote, J., Beautrais, A., Currier, D., Haas, A. et al. (2005). Suicide prevention strategies: a systematic review. *JAMA, 294,* 2064-2074.

Mann, J. J., Waternaux, C., Haas, G. L., & Malone, K. M. (1999). Toward a clinical model of suicidal behavior in psychiatric patients. *American Journal of Psychiatry, 156,* 181-189.

Maris, R. W. (2002). Suicide. *Lancet, 360,* 319-326.

Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T. (2005). Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Archives of General Psychiatry, 62,* 975-983.

Marzuk, P. M., Hartwell, N., Leon, A. C., & Portera, L. (2005). Executive functioning in depressed patients with suicidal ideation. *Acta Psychiatrica Scandinavica, 112,* 294-301.

Matthews, C. G. & Kløve, H. (1964). *Instruction Manual for the Adult Neuropsychology Test Battery*. Madison, WI: University of Wisconsin Medical school.

McCleery, A., Addington, J., & Addington, D. (2006). Substance misuse and cognitive functioning in early psychosis: a 2 year follow-up. *Schizophrenia Research, 88,* 187-191.

McGirr, A., Renaud, J., Bureau, A., Seguin, M., Lesage, A., & Turecki, G. (2008). Impulsive-aggressive behaviours and completed suicide across the life cycle: a predisposition for younger age of suicide. *Psychological Medicine, 38,* 407-417.

McGirr, A., Tousignant, M., Routhier, D., Pouliot, L., Chawky, N., Margolese, H. C. et al. (2006). Risk factors for completed suicide in schizophrenia and other chronic psychotic disorders: a case-control study. *Schizophrenia Research, 84,* 132-143.

McGirr, A. & Turecki, G. (2008). What is specific to suicide in schizophrenia disorder? Demographic, clinical and behavioural dimensions. *Schizophrenia Research, 98,* 217-224.

McGlashan, T. H. (1999). Duration of untreated psychosis in first-episode schizophrenia: marker or determinant of course? *Biological Psychiatry, 46,* 899-907.

McGorry, P. D., Killackey, E., & Yung, A. R. (2007). Early intervention in psychotic disorders: detection and treatment of the first episode and the critical early stages. *Medical Journal of Australia, 187,* S8-10.

McGorry, P. D. & McConville, S. B. (1999). Insight in psychosis: an elusive target. *Comprehensive Psychiatry, 40,* 131-142.

McGrath, J., Saha, S., Chant, D., & Welham, J. (2008). Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiologic Reviews, 30,* 67-76.

McGrath, J., Saha, S., Welham, J., El, S. O., MacCauley, C., & Chant, D. (2004). A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC.Medicine., 2,* 13.

McKenzie, K., Serfaty, M., & Crawford, M. (2003). Suicide in ethnic minority groups. *British Journal of Psychiatry, 183,* 100-101.

McKeon, R. (2009). *Suicidal behavior*. Cambridge, Massachusetts: Hogrefe & Huber Publishers.

Melle, I., Johannesen, J. O., Friis, S., Haahr, U., Joa, I., Larsen, T. K. et al. (2006). Early detection of the first episode of schizophrenia and suicidal behavior. *American Journal of Psychiatry, 163,* 800-804.

Melle, I., Larsen, T. K., Haahr, U., Friis, S., Johannesen, J. O., Opjordsmoen, S. et al. (2008). Prevention of negative symptom psychopathologies in first-episode schizophrenia: two-year effects of reducing the duration of untreated psychosis. *Archives of General Psychiatry, 65,* 634-640.

Melle, I., Larsen, T. K., Haahr, U., Friis, S., Johannessen, J. O., Opjordsmoen, S. et al. (2004). Reducing the duration of untreated first-episode psychosis: effects on clinical presentation. *Archives of General Psychiatry, 61,* 143-150.

Meltzer, H. Y., Alphs, L., Green, A. I., Altamura, A. C., Anand, R., Bertoldi, A. et al. (2003). Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (InterSePT). *Archives of General Psychiatry, 60,* 82-91.

Mintz, A. R., Dobson, K. S., & Romney, D. M. (2003). Insight in schizophrenia: a meta-analysis. *Schizophrenia Research, 61,* 75-88.

Montross, L. P., Zisook, S., & Kasckow, J. (2005). Suicide among patients with schizophrenia: a consideration of risk and protective factors. *Annals of Clinical Psychiatry, 17,* 173-182.

Mueser, K. T. & McGurk, S. R. (2004). Schizophrenia. *Lancet, 363,* 2063-2072.

Nangle, J. M., Clarke, S., Morris, D. W., Schwaiger, S., McGhee, K. A., Kenny, N. et al. (2006). Neurocognition and suicidal behaviour in an Irish population with major psychotic disorders. *Schizophrenia Research, 85,* 196-200.

Nielssen, O. B. & Large, M. M. (2009). Untreated psychotic illness in survivors of violent suicide attempts. *Early Intervention in Psychiatry, 3,* 116-122.

Nordentoft, M. (2007). Prevention of suicide and attempted suicide in Denmark. Epidemiological studies of suicide and intervention studies in selected risk groups. *Danish Medical Bulletin, 54,* 306-369.

Nordentoft, M., Jeppesen, P., Abel, M., Kassow, P., Petersen, L., Thorup, A. et al. (2002). OPUS study: suicidal behaviour, suicidal ideation and hopelessness among patients with first-episode psychosis. One-year follow-up of a randomised controlled trial. *British Journal of Psychiatry.Supplement, 43,* s98-106.

Norwegian Institute of Public Health (2009). Selvmord - faktaark. [On-line]. Available: http://www.fhi.no/artikler?id=45617

Olfson, M., Marcus, S. C., Wilk, J., & West, J. C. (2006). Awareness of illness and nonadherence to antipsychotic medications among persons with schizophrenia. *Psychiatric Services, 57,* 205-211.

Owens, D., Horrocks, J., & House, A. (2002). Fatal and non-fatal repetition of self-harm. Systematic review. *British Journal of Psychiatry, 181,* 193-199.

Palmer, B. A., Pankratz, V. S., & Bostwick, J. M. (2005). The lifetime risk of suicide in schizophrenia: a reexamination. *Archives of General Psychiatry, 62,* 247-253.

Patel, J. K., Pinals, D. A., & Breier, A. (2008). Schizophrenia and other psychoses. In A.Tasman, J. Kay, J. A. Lieberman, M. B. First, & M. Maj (Eds.), *Psychiatry* (3 ed., pp. 1201-1282). Chichester: Wiley-Blackwell.

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology, 51,* 768-774.

Pedersen, G., Hagtvet, K. A., & Karterud, S. (2007). Generalizability studies of the Global Assessment of Functioning-Split version. *Comprehensive Psychiatry, 48,* 88-94.

Pekkala, E. & Merinder, L. (2002). Psychoeducation for schizophrenia. *Cochrane.Database.Syst.Rev.,* CD002831.

Pencer, A. & Addington, J. (2003). Substance use and cognition in early psychosis. *Journal of Psychiatry and Neuroscience, 28,* 48-54.

Perala, J., Suvisaari, J., Saarni, S. I., Kuoppasalmi, K., Isometsa, E., Pirkola, S. et al. (2007). Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Archives of General Psychiatry, 64,* 19-28.

Perkins, D. O., Gu, H., Boteva, K., & Lieberman, J. A. (2005). Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. *American Journal of Psychiatry, 162,* 1785-1804.

Pini, S., Cassano, G. B., Dell'Osso, L., & Amador, X. F. (2001). Insight into illness in schizophrenia, schizoaffective disorder, and mood disorders with psychotic features. *American Journal of Psychiatry, 158,* 122-125.

Pompili, M., Amador, X. F., Girardi, P., Harkavy-Friedman, J., Harrow, M., Kaplan, K. et al. (2007). Suicide risk in schizophrenia: learning from the past to change the future. *Annals of General Psychiatry, 6,* 10.

Potkin, S. G., Anand, R., Alphs, L., & Fleming, K. (2003). Neurocognitive performance does not correlate with suicidality in schizophrenic and schizoaffective patients at risk for suicide. *Schizophrenia Research, 59,* 59-66.

Preston, E. & Hansen, L. (2005). A systematic review of suicide rating scales in schizophrenia. *Crisis, 26,* 170-180.

Preti, A., Meneghelli, A., Pisano, A., & Cocchi, A. (2009). Risk of suicide and suicidal ideation in psychosis: results from an Italian multi-modal pilot program on early intervention in psychosis. *Schizophrenia Research, 113,* 145-150.

Pritchard, C. & Hansen, L. (2005). Comparison of suicide in people aged 65-74 and 75+ by gender in England and Wales and the major Western countries 1979-1999. *International Journal of Geriatric Psychiatry, 20,* 17-25.

Radomsky, E. D., Haas, G. L., Mann, J. J., & Sweeney, J. A. (1999). Suicidal behavior in patients with schizophrenia and other psychotic disorders. *American Journal of Psychiatry, 156,* 1590-1595.

Raust, A., Slama, F., Mathieu, F., Roy, I., Chenu, A., Koncke, D. et al. (2007). Prefrontal cortex dysfunction in patients with suicidal behavior. *Psychological Medicine, 37,* 411-419.

Restifo, K., Harkavy-Friedman, J. M., & Shrout, P. E. (2009). Suicidal behavior in schizophrenia: a test of the demoralization hypothesis. *Journal of Nervous and Mental Disease, 197,* 147-153.

Ringen, P. A., Melle, I., Birkenaes, A. B., Engh, J. A., Faerden, A., Jonsdottir, H. et al. (2008). Illicit drug use in patients with psychotic disorders compared with that in the general population: a cross-sectional study. *Acta Psychiatrica Scandinavica, 117,* 133-138.

Ringen, P. A., Vaskinn, A., Sundet, K., Engh, J. A., Jonsdottir, H., Simonsen, C. et al. (2010). Opposite relationships between cannabis use and neurocognitive functioning in bipolar disorder and schizophrenia. *Psychological Medicine, 40,* 1337-1347.

Robinson, J., Cotton, S., Conus, P., Schimmelmann, B. G., McGorry, P., & Lambert, M. (2009). Prevalence and predictors of suicide attempt in an incidence cohort of 661 young people with first-episode psychosis. *Australian and New Zealand Journal of Psychiatry, 43,* 149-157.

Romm, K. L., Rossberg, J. I., Berg, A. O., Barrett, E. A., Faerden, A., Agartz, I. et al. (2010). Depression and depressive symptoms in first episode psychosis. *Journal of Nervous and Mental Disease, 198,* 67-71.

Rosenheck, R., Leslie, D., Keefe, R., McEvoy, J., Swartz, M., Perkins, D. et al. (2006). Barriers to employment for people with schizophrenia. *American Journal of Psychiatry, 163,* 411-417.

Rush, A. J., Gullion, C. M., Basco, M. R., Jarrett, R. B., & Trivedi, M. H. (1996). The Inventory of Depressive Symptomatology (IDS): psychometric properties. *Psychological Medicine, 26,* 477-486.

Saha, S., Chant, D., & McGrath, J. (2007). A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Archives of General Psychiatry, 64,* 1123-1131.

Salmon, P. (2000). *Psychology of medicine and surgery: a guide for psychologists, cousellors, nurses, and doctors.* Chichester: J. Wiley.

Schwartz, R. C. & Smith, S. D. (2004). Suicidality and psychosis: the predictive potential of symptomatology and insight into illness. *Journal of Psychiatric Research, 38,* 185-191.

Seeman, M. V. (2007). An outcome measure in schizophrenia: mortality. *Canadian Journal of Psychiatry.Revue Canadienne de Psychiatrie, 52,* 55-60.

Silverman, M. M. (2006). The language of suicidology. *Suicide and Life-Threatening Behavior, 36,* 519-532.

Silverman, M. M., Berman, A. L., Sanddal, N. D., O'carroll, P. W., & Joiner, T. E. (2007). Rebuilding the tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 1: Background, rationale, and methodology. *Suicide and Life-Threatening Behavior, 37,* 248-263.

Skegg, K. (2005). Self-harm. *Lancet, 366,* 1471-1483.

Staring, A. B., Van der Gaag, M., Van den Berge, M., Duivenvoorden, H. J., & Mulder, C. L. (2009). Stigma moderates the associations of insight with depressed mood, low self-esteem, and low quality of life in patients with schizophrenia spectrum disorders. *Schizophrenia Research, 115,* 363-369.

Startup, M. (1997). Awareness of own and others' schizophrenic illness. *Schizophrenia Research, 26,* 203-211.

Steblaj, A., Tavcar, R., & Dernovsek, M. Z. (1999). Predictors of suicide in psychiatric hospital. *Acta Psychiatrica Scandinavica, 100,* 383-388.

Sundet, K. & Vaskinn, A. (2008). Estimating premorbid IQ. (Article in Norwegian, abstract in English). *Journal of Norwegian Psychological Association, 9,* 1108-1115.

Swann, A. C., Dougherty, D. M., Pazzaglia, P. J., Pham, M., Steinberg, J. L., & Moeller, F. G. (2005). Increased impulsivity associated with severity of suicide attempt history in patients with bipolar disorder. *American Journal of Psychiatry, 162,* 1680-1687.

Tandon, R., Nasrallah, H. A., & Keshavan, M. S. (2009). Schizophrenia, "just the facts" 4. Clinical features and conceptualization. *Schizophrenia Research, 110,* 1-23.

Tarrier, N., Khan, S., Cater, J., & Picken, A. (2007). The subjective consequences of suffering a first episode psychosis: trauma and suicide behaviour. *Social Psychiatry and Psychiatric Epidemiology, 42,* 29-35.

Torrey, E. F. (2002). Studies of individuals with schizophrenia never treated with antipsychotic medications: a review. *Schizophrenia Research, 58,* 101-115.

van Os, J. & Kapur, S. (2009). Schizophrenia. *Lancet, 374,* 635-645.

Verdoux, H., Liraud, F., Gonzales, B., Assens, F., Abalan, F., & van, O. J. (1999). Suicidality and substance misuse in first-admitted subjects with psychotic disorder. *Acta Psychiatrica Scandinavica, 100,* 389-395.

Verdoux, H., Liraud, F., Gonzales, B., Assens, F., Abalan, F., & van, O. J. (2001). Predictors and outcome characteristics associated with suicidal behaviour in early psychosis: a two-year follow-up of first-admitted subjects. *Acta Psychiatrica Scandinavica, 103,* 347-354.

Wasserman, D., Cheng, Q., & Jiang, G. X. (2005). Global suicide rates among young people aged 15-19. *World Psychiatry, 4,* 114-120.

Watson, P. W., Garety, P. A., Weinman, J., Dunn, G., Bebbington, P. E., Fowler, D. et al. (2006). Emotional dysfunction in schizophrenia spectrum psychosis: the role of illness perceptions. *Psychological Medicine, 36,* 761-770.

Wechsler, D. (2003). *Wechsler Adult Intelligence Scale - Third edition (WAIS-III). Norwegian Manual.* Stockholm: Pearson Assessment.

Wechsler, D. (2007). *Wechsler Abbreviated Scale of Intelligence (WASI). Norwegian Manual supplement.* Stockholm: Pearson Assessment.

Westermeyer, J. F., Harrow, M., & Marengo, J. T. (1991). Risk for suicide in schizophrenia and other psychotic and nonpsychotic disorders. *Journal of Nervous and Mental Disease, 179,* 259-266.

Westheide, J., Quednow, B. B., Kuhn, K. U., Hoppe, C., Cooper-Mahkorn, D., Hawellek, B. et al. (2008). Executive performance of depressed suicide attempters: the role of suicidal ideation. *European Archives of Psychiatry and Clinical Neuroscience, 258,* 414-421.

WHO (1993). *The ICD-10 Classification of Mental and Behavioural Disorders. Diagnostic Criteria for Research*. Geneva: World Health Organization.

WHO (2010). Suicide prevention. [On-line]. Available: http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/index.html

Wiffen, B. D., Rabinowitz, J., Lex, A., & David, A. S. (2010). Correlates, change and 'state or trait' properties of insight in schizophrenia. *Schizophrenia Research*.

Williams, J. M. G., Crane, C., Barnhofer, T., & Duggan, D. (2005). Psychology and suicidal behaviour: elaborating the entrapment model. In K.Hawton (Ed.), *Prevention and treatment of suicidal beahviour* (pp. 71-89). New York: Oxford University Press.

Wobrock, T., Sittinger, H., Behrendt, B., D'Amelio, R., Falkai, P., & Caspari, D. (2007). Comorbid substance abuse and neurocognitive function in recent-onset schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience, 257,* 203-210.

Woodberry, K. A., Giuliano, A. J., & Seidman, L. J. (2008). Premorbid IQ in schizophrenia: a meta-analytic review. *American Journal of Psychiatry, 165,* 579-587.

Wu, C. S., Liao, S. C., Lin, K. M., Tseng, M. M., Wu, E. C., & Liu, S. K. (2009). Multidimensional assessments of impulsivity in subjects with history of suicidal attempts. *Comprehensive Psychiatry, 50,* 315-321.

Zahl, D. L. & Hawton, K. (2004). Repetition of deliberate self-harm and subsequent suicide risk: long-term follow-up study of 11,583 patients. *British Journal of Psychiatry, 185,* 70-75.

Zisook, S., Byrd, D., Kuck, J., & Jeste, D. V. (1995). Command hallucinations in outpatients with schizophrenia. *Journal of Clinical Psychiatry, 56,* 462-465.

APPENDIX 1

Vignette A

Holdninger og oppfatninger om psykiske problemer. (EAB 15.03.06)

Dette spørreskjemaet handler om en hypotetisk person som heter Ola. I boksen nedenfor beskrives hvordan han har hatt det den siste tiden.

Ola er 24 år og bor hjemme hos foreldrene sine. Han har hatt noen få midlertidige jobber siden han sluttet på skolen, men er arbeidsledig nå. I løpet av de siste seks månedene har han sluttet å være sammen med vennene sine. Han har begynt å låse seg inne på soverommet og nekter å spise sammen med familien eller å bade. Foreldrene hans kan også høre at han går omkring på soverommet sitt om natten etter at de har lagt seg. Selv om de vet at han er alene, har de hørt at han roper og krangler som om det er noen andre der. Når de prøver å oppmuntre ham til å gjøre ting, hvisker han at han ikke vil forlate huset fordi naboene spionerer på ham. De tror ikke at han tar stoff, for han aldri er sammen med andre eller går noen steder.

1. Ut fra informasjonen over, hva er galt med Ola, hvis noe?

   .....

   .....

2. Tror du Ola trenger profesjonell hjelp? ☐Ja ☐Nei

3. Hvis Ola skulle søke hjelp fra noen av de følgende personene, er det sannsynlig at det vil hjelpe Ola, være skadelig for ham, eller ingen av delene? (*Sett ett kryss for hver linje*)

	Til hjelp	*Ingen av delene*	*Skadelig*
a. En vanlig allmennpraktiserende lege eller fastlege	☐1	☐2	☐3
b. En vanlig apoteker	☐1	☐2	☐3
c. En rådgiver	☐1	☐2	☐3
d. En sosialarbeider	☐1	☐2	☐3
e. Hjelpetelefon, f.eks. Mental Helse	☐1	☐2	☐3
f. En psykiater	☐1	☐2	☐3
g. En klinisk psykolog	☐1	☐2	☐3
h. Hjelp fra hans nære familie	☐1	☐2	☐3
i. Hjelp fra nære venner	☐1	☐2	☐3
j. En homeopat eller urtekyndig	☐1	☐2	☐3
k. En prest	☐1	☐2	☐3
l. Ola prøver å takle problemene sine på egenhånd	☐1	☐2	☐3

4. Hvis Ola skulle ta en av de følgende medisinene, er det sannsynlig at det vil hjelpe Ola, være skadelig for ham, eller ingen av delene? (*Sett ett kryss for hver linje*)

	Til hjelp	*Ingen av delene*	*Skadelig*
a. Vitaminer og mineraler, kosttilskudd eller urtemedisin	☐1	☐2	☐3
b. Smertestillende midler	☐1	☐2	☐3
Antidepressiva/midler mot depresjon	☐1	☐2	☐3
d. Antibiotika	☐1	☐2	☐3
e. Beroligende midler/sovemidler	☐1	☐2	☐3
f. Antipsykotiske midler	☐1	☐2	☐3
g. Angstdempende midler	☐1	☐2	☐3

5. Hvis Ola skulle foreta seg noe av det følgende, er det sannsynlig at det vil hjelpe Ola, være skadelig for ham, eller ingen av delene? (*Sett ett kryss for hver linje*)

	Til hjelp	*Ingen av delene*	*Skadelig*
a. Bli mer fysisk aktiv	☐1	☐2	☐3
b. Lese selvhjelps bøker	☐1	☐2	☐3
c. Komme seg mer ut	☐1	☐2	☐3
d. Kurs i avslapning, håndtering av stress, meditasjon eller yoga	☐1	☐2	☐3
e. Slutte å drikke alkohol	☐1	☐2	☐3
f. Rådgivning	☐1	☐2	☐3
g. Psykoterapi/samtalebehandling	☐1	☐2	☐3
h. Hypnose	☐1	☐2	☐3
i. Innleggelse på psykiatrisk sykehusavdeling	☐1	☐2	☐3
j. Elektrosjokk behandling (ECT)	☐1	☐2	☐3
k. Drikke litt alkohol av og til for å slappe av	☐1	☐2	☐3
l. En spesiell diett eller unngå visse typer mat	☐1	☐2	☐3

6. Hva ville bli det sannsynlige resultatet hvis Ola fikk den type profesjonell hjelp du synes er mest riktig? *(Sett kun ett kryss)*

- ☐ Fullstendig bedring uten videre problemer
- ☐ Fullstendig bedring, men problemer ville sannsynligvis komme igjen
- ☐ Delvis bedring
- ☐ Delvis bedring, men problemer ville sannsynligvis komme igjen
- ☐ Ingen bedring
- ☐ Bli verre

7. Hva ville bli det sannsynlige resultatet hvis Ola **ikke** fikk profesjonell hjelp? *(Sett kun ett kryss)*

- ☐ Fullstendig bedring uten videre problemer
- ☐ Fullstendig bedring, men problemer ville sannsynligvis komme igjen
- ☐ Delvis bedring
- ☐ Delvis bedring, men problemer ville sannsynligvis komme igjen
- ☐ Ingen bedring
- ☐ Bli verre

8. Anta at Ola fikk den hjelpen du synes er riktigst for hans psykiske problemer. Hvordan tror du han vil fremstå **på lang sikt** sammenlignet med andre mennesker i samfunnet? Hvor sannsynlig er det at han: (*Sett ett kryss for hver linje*)

		Mer sannsynlig	*Like sannsynlig*	*Mindre sannsynlig*
a.	er voldelig	☐1	☐2	☐3
b.	drikker for mye	☐1	☐2	☐3
c.	tar ulovlige narkotiske stoffer	☐1	☐2	☐3
d.	har dårlige venneforhold	☐1	☐2	☐3
e.	prøver å ta sitt eget liv	☐1	☐2	☐3
f.	er forståelsesfull i forhold til andre menneskers følelser	☐1	☐2	☐3
g.	har et godt ekteskap	☐1	☐2	☐3
h.	er en omsorgsfull forelder	☐1	☐2	☐3
i.	er en produktiv arbeidstager	☐1	☐2	☐3
j.	er kreativ eller kunstnerisk	☐1	☐2	☐3

9. Tror du Ola ville bli diskriminert av andre i samfunnet hvis de visste om problemene han har hatt?

☐ Ja ☐ Nei

I

II

III